AN INVESTIGATION INTO THE LEUCOCYTOSIS OF TYPHUS FEVER WITH OBSERVATIONS ON THE CHANGES PRESENT IN THE BONE MARROW, SPLEEN AND LYMPHOID TISSUES

Being a Thesis for the Degree of Doctor of Medicine presented to the University of Glasgow

by

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DESCRIPTION OF PLATE I

Fig. 1. Blood from Case No. IV showing polymorpho-nuclear leucocytes. Film fixed by heat: Ehrlich's tri-acid stain.

Fig. 2. Same Case - showing polymorpho-nuclear leucocytes, lymphocytes and large mono-nuclear cells. Film fixed by heat: Ehrlich's triacid stain.

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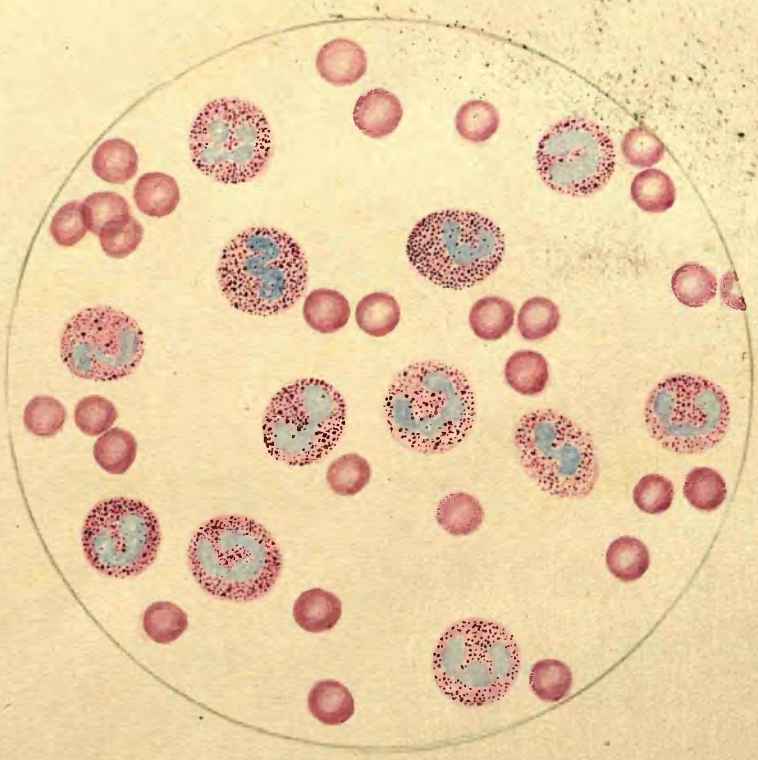

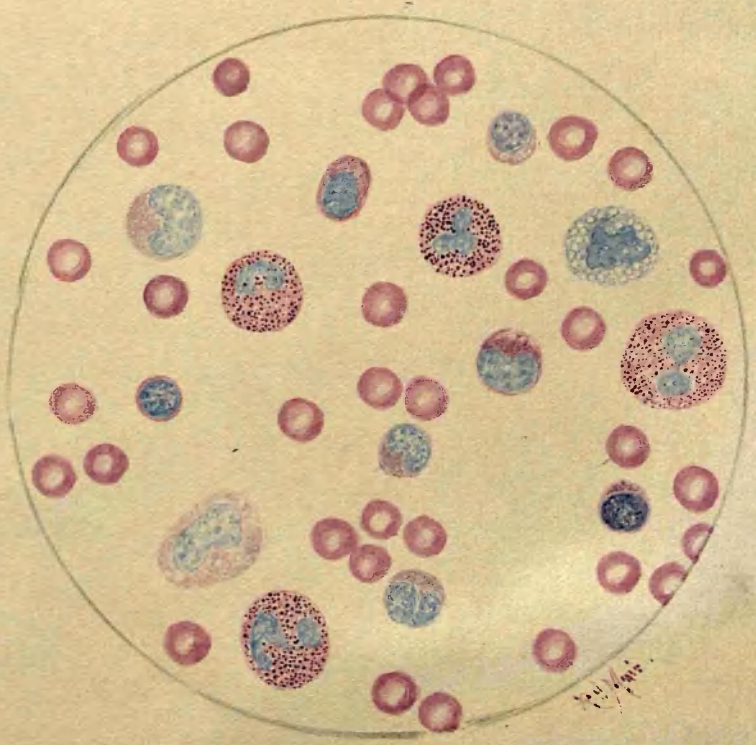

Blood film. (Carriage)

Syphilis

×1000 dia

Blood film (Carriage)

Syphilis - ×1000 dia

DESCRIPTION OF PLATE II

Fig. 1. Blood from Case No. IV showing eosinophiles. Film fixed by heat: Ehrlich's triacid stain.

Fig. 2. Blood from a fatal case (Case No. VIII) showing polymorpho-nuclear corpuscles, one of which is vacuolated, lymphocytes, and large mono-nuclear cells. No eosinophiles. Film fixed by heat: Ehrlich's triacid stain.

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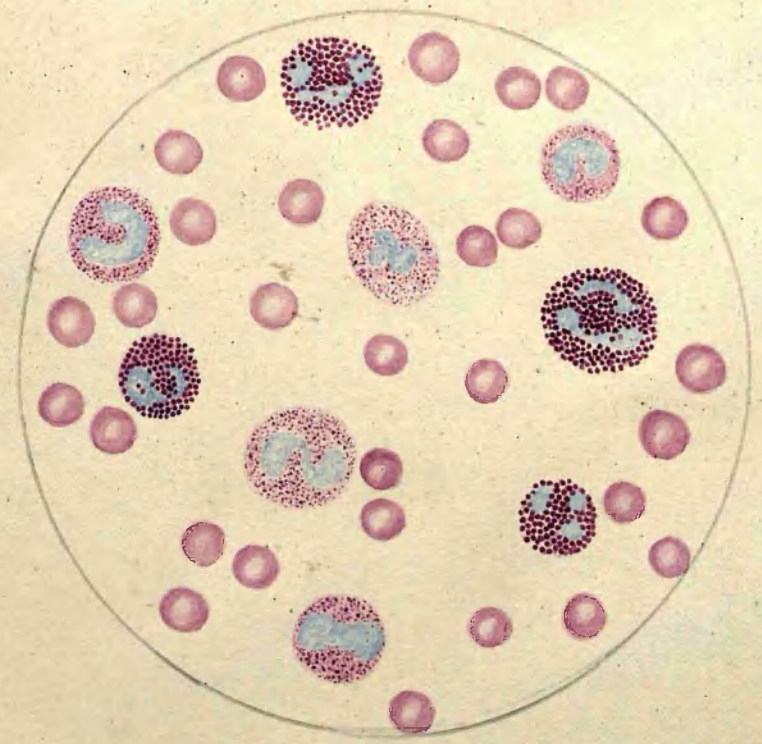

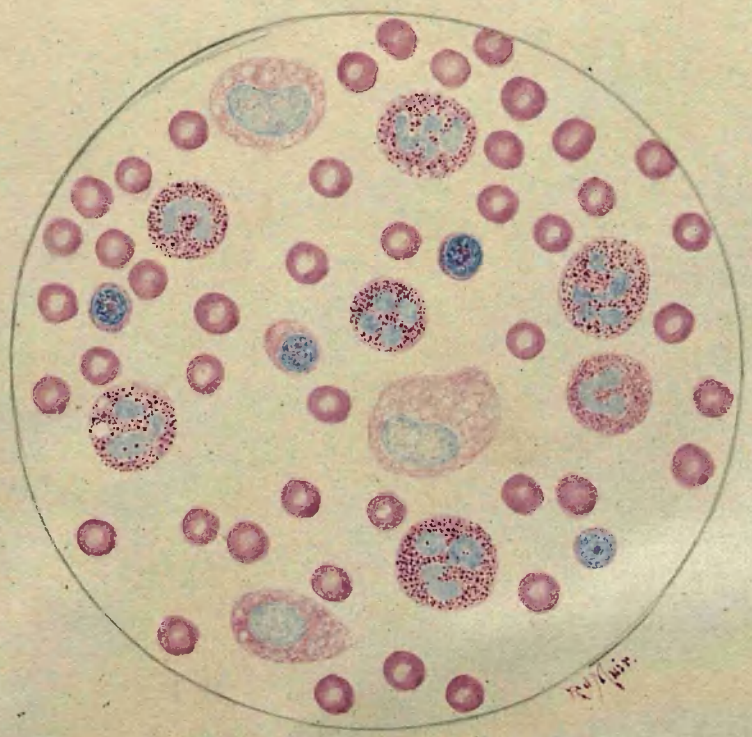

Blood film - (Carrigan).

Syphilis

x 1000 diam.

Blood film (Elliot)

Syphilis

x 1000 diam.

AN INVESTIGATION into the leucocytosis of Typhus Fever, with Observations on the Changes present in the Bone Marrow, Spleen, and Lymphoid Tissues

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The physiological importance of the white blood corpuscles has for some time been fully recognised, but the significance of the changes presented by these in various pathological conditions has been the subject of the most recent researches only.

The result of these investigations has been the discovery of many interesting phenomena connected with the leucocytes, and more especially of the condition known as leucocytosis.

These discoveries have led to the publication of a great amount of literature on hematology, and to the evolution of a number of theories which seek to explain the significance of this symptom.

The two best known of these which deal with this point are those of Phagocytosis and Chemiotaxis, advanced by Metschnikoff and Pfeffer respectively.

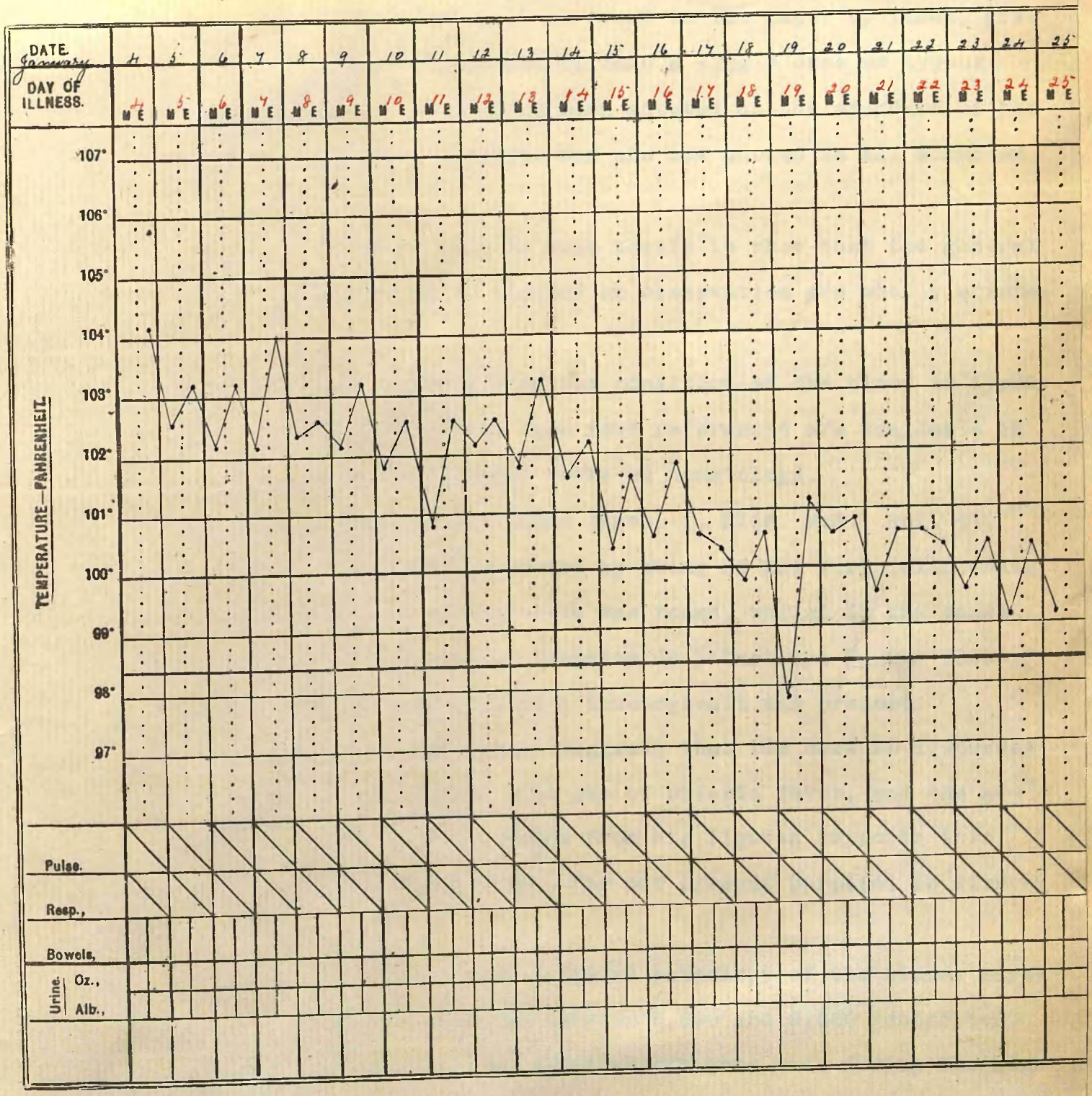
Metschnikoff's theory is to the effect that the leucocytes defend the organism against bacteria by imprisoning them by the aid of their pseudopodia, taking them up into their substance, and so depriving them of the power of injuriously affecting the surrounding

tissues, whilst the principle of chemiotaxis promulgated by Pfeffer asserts that bacteria, or rather their metabolic products, are able to attract by chemical influence the cells stored up in the blood-forming organs, and so increasing the number in the blood stream (positive chemiotaxis); in those cases, on the other hand, in which there is a reduction in the number of leucocytes in the blood, this phenomenon results from a repulsive action on the leucocytes displayed by the chemical bodies mentioned (negative chemiotaxis).

For the purposes of this thesis it is sufficient to mention here that these theories have a distinct bearing on the subject under investigation, a connection which will be discussed in detail later.

Many observations on the clinical importance of leucocytosis in infectious diseases and their various stages have been accumulated and published. Some of these are incomplete, while other published results deal with only one or two cases, or merely with isolated observations made at different stages of the disease.

If errors are to be avoided, it is necessary to collect a large series of general observations, made at regular intervals, and throughout the whole course of the disease, as the most far-reaching and erroneous conclusions on the general pathology of the blood have sometimes been deduced from the investigation of a single case. As an illustration of this statement, Troje's paper may be mentioned (Uber Leukemie und Pseudoleukemie, Berl. Klin. Woch. 1892, No. 12). In this publication he failed to recognise the lymphocytic character of the case of leukemia he dealt with, and, believing it to be one of myelogenous origin, this observer denied and completely reversed all that had been previously established by others with reference to


DATE. January
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
DAY OF ILLNESS.
4 ME 5 ME 6 ME 7 ME 8 ME 9 ME 10 ME 11 ME 12 ME 13 ME 14 ME 15 ME 16 ME 17 ME 18 ME 19 ME 20 ME 21 ME 22 ME 23 ME 24 ME 25 ME
TEMPERATURE—FAHRENHEIT.
107°
106°
105°
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103°
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101°
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99°
98°
97°
Pulse.
Resp.,
Bowels,
Urine. Oz.,
Alb.,

this disease.

A second illustration will be found in the paper by Tumas, giving the results of an investigation into a single case of typhus fever. These results have since been adopted as the standard of the blood condition in that disease, and are now quoted in all works on hematology.

An attempt will be made in this thesis to show that the general conclusions deduced from so limited an observation are wholly erroneous.

The literature dealing with the condition of the blood in typhus fever is very limited, indeed only four references are available in either the older or more recent works on hematology.

In one case observed by Tumas (Arch. f. Klin. Med., vol. 41, p. 363), and in four cases observed by Ewing of New York (Clin. Path. of the Blood 1901), no leucocytosis was found, whilst in the cases observed by Everard and Demoor (Annales de l'Institut Pasteur 1893), and by Wilks (Sajous Annual 1895), leucocytosis was present.

An analysis of Tumas' paper suggests that the case he discusses was not really one of typhus, but one of enteric fever, and the accompanying temperature chart drawn from his figures supports this suspicion, so that this case may, for our present purpose, be disregarded.

Ewing, in his work on the clinical pathology of the blood, says, "In four cases the writer found between 5,000 and 9,000 leucocytes. "The patients were adults, the examinations were made during the high "fever of the early period of the disease, and at least two of the "patients died." This somewhat general statement is all the informa-

tion that this author offers on the subject. He examined four cases, and these only during the early period of the disease, so that his conclusions may also, to a certain extent, be disregarded.

In the short paragraph devoted to typhus fever in "Cabot", a reference is given to an article by Everard and Demoor in the "Annales de l'Institut Pasteur" February 1893, stating that these observers found leucocytosis present in typhus fever, but, although careful search was made throughout this article, no mention whatever of typhus blood could be found. In the British Medical Journal (December 1883), there is an article by Mott of London, and Blore of Liverpool on "Micro-organisms in Typhus Fever". These observers make a statement in the course of their article which is of great importance in its bearing on the present subject. They say, "Another fact "noted about the blood was a great increase of the white corpuscles". We are thus practically without any detailed and accurate literature on the subject of leucocytosis in typhus fever.

A few isolated observations made by myself in the city of Glasgow Fever Hospital, Belvidere, led me to form the opinion that leucocytosis is present in typhus fever, and the occurrence of a limited epidemic in Glasgow in the autumn of 1902, afforded an opportunity of making more extended observations, with which I now propose to deal.

In the first few cases, the observations were limited in their range owing to the fact that the patients were admitted to hospital only after the disease was well advanced, but, in the later cases, as a result of the precautions of the Sanitary Authorities, which enabled them to remove patients into hospital on the first appearance

of symptoms, it was possible to carry on the observations on the blood from the first day of illness till the termination of the attack.

In carrying out the routine observations, and with the object of limiting, as far as possible, errors resulting from physiological leucocytosis, two examinations of the blood were made daily - the first between 11 a.m. and 12 noon, and the second between 8.30 p.m. and 9.30 p.m. The leucocytes were counted both morning and evening, the red corpuscles in the morning only.

The blood was usually taken, without pressure, from the lobe of the ear, but occasionally it was found more convenient to collect it from the finger. Films were prepared at the same time for fixing and staining. For the estimation of the corpuscles the Thoma-Zeiss Hemocytometer was used. For diluting the blood in estimating the number of red cells, the fluid recommended by Gowers, composed of sulphate of soda, acetic acid, and water was mostly employed, but occasionally Toisson's fluid, consisting of chloride of sodium, sulphate of soda, methyl violet, glycerine, and water was substituted. The former of these was found, as a rule, the more suitable.

In estimating the red corpuscles, the average number of squares counted was 128; in many cases this was done two or three times in order to ensure accuracy. For the same reason, several estimates of the white cells were made, care being taken to secure uniformity of dilution by frequently agitating the contents of the pipette, and by carrying out each observation as expeditiously as was consistent with accuracy of result. The diluting solution used in counting the white corpuscles was $\frac{1}{2}\%$ solution of acetic acid tinged with methyl blue.

The films of blood were allowed to dry in the air, fixed by heat, and stained with Ehrlich's triacid stain. In fixing, an oven was employed, so that the temperature might be accurately regulated. The best results were obtained by fixing at a temperature of 115°C., maintained for forty minutes.

In the course of the present investigation into the condition of the blood in typhus fever, 670 counts of the white corpuscles, and 270 counts of the red corpuscles were made, while 333 differential leucocyte counts were made from stained films, and a number of samples of fresh blood without preparation were also examined. The patients examined were male and female adults, adolescents, and young children, so that the results indicate the influence both of sex and age upon the leucocytosis, and the condition of the red cells.

The characters of the serum were likewise investigated so far, at least, as its power of causing agglutination of the typhoid bacillus and allied organisms is concerned, and it is proposed to include the results of these last observations in the discussion.

Finally, it may be stated that the results were frequently checked by my colleagues in hospital, as well as by the expedient of making estimates of the same blood both with the pipette used for the red cells, and with that used for the leucocytes. In the differentiation of the leucocytes, an average of 400 was counted in each stained film, and for this purpose the mechanical stage was employed.

For the sake of simplicity, it has been thought best to divide the cases into two groups, the first of which includes all the fatal cases, and the second all those that recovered. The former group comprises 9, and the latter 17 cases.

Of the fatal cases 8 were females, their ages ranging from 1½ to 56 years; the remaining fatality occurred in a male, aged 45 years. Of those who recovered, 7 were females, their ages ranging from 6 to 22 years, whilst 10 were males with ages ranging from 6 months to 61 years.

The blood condition in typhus, as in other diseases, can be profitably studied only when taken in association with the other clinical conditions present in the case, and it has, therefore, been thought advisable to present a short clinical sketch of each case, including its progress and result, with a chart of the differential estimates of white and red cells. The more general conclusions and extended tables will be left for later discussion.

The nomenclature employed in the text is that adopted by Ehrlich so that the terms Polymorpho-nuclear, Large Mono-nuclear, Lymphocyte, and Eosinophile are used in their familiar signification.

GROUP I - FATAL CASES

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CASE 1. Mrs. A., aet. 36, was admitted to hospital on 15th October 1902, having been ill for twelve days. On admission her temperature was 104.6° F., pulse rate 134, and respirations 36 per minute.

She was very ill and delirious. Her scalp, face, and skin generally presented a dusky appearance; her conjunctivae were suffused, and her pupils contracted. The tongue was dry, brownish red in colour, and lightly fissured. The pulse was weak and thready. Over the trunk and limbs there was a fairly profuse typhus eruption, the mulberry spots being fixed, and best marked on the abdomen, and down the outer sides of the thighs. On the back of the head and on the right buttock respectively there was a patch of subcutaneous hemorrhage about the size of a florin.

There was some fine tremor of the hands, and marked subsultus tendinum.

Examination of the chest revealed no organic disease of the heart, but snoring rhonci were heard all over the lungs, and a few sub-crepitant râles at both bases behind.

She gradually sank, and died on the morning of 17th October, about 30 hours after admission to hospital.

Only one leucocyte estimation was possible, and it gave 8,000 cells per c.m., a condition practically normal, and indicating but

FATAL CASES Contd.

little or no reaction on the part of the blood-forming organs to the toxine of the fever. No differential count was made. Unfortunately, a post-mortem examination was not permitted.

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CASE NO. 1. Mrs. A. (aet. 30) admitted to hospital on eleventh day of illness. Died on the thirteenth day of illness.

Date Oct.	Day of Illness	Temperatures M	E	Leucocytes
16	12	105.	103.8	8,000

Hb
R.B.C ?

EXPLANATION OF CHART

Leucocytes in Black

Temperature in Red

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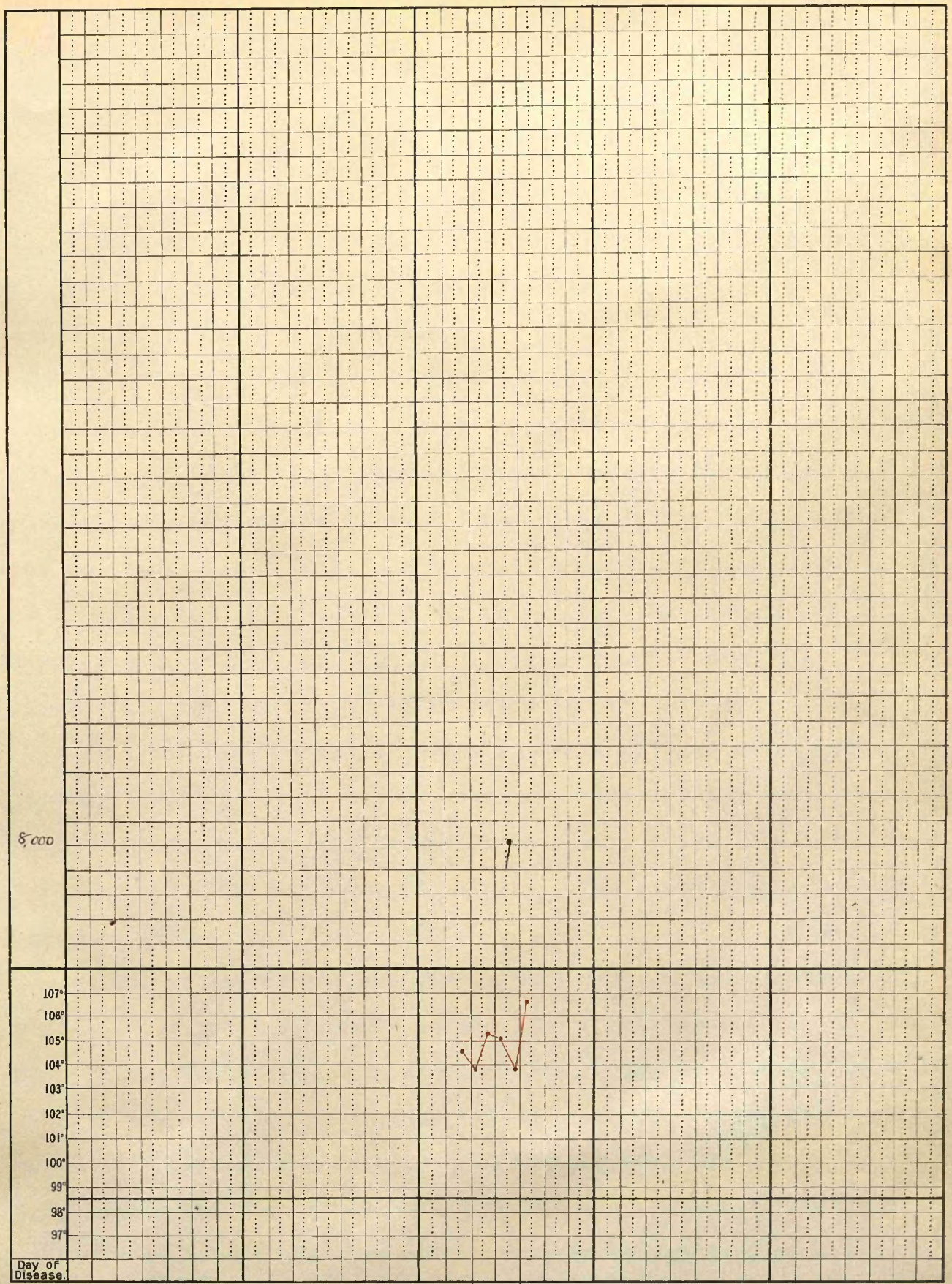
Chart I.



FATAL CASES Contd.

CASE 2. Matilda A., a daughter of the first patient, aet. 1½ years, was admitted to hospital on 20th October 1902. She had been in the reception house as a "Contact" whence, her temperature having risen, she was removed to hospital.

On admission, her temperature was 101° F., pulse rate 184, and respirations 28 per minute. There was a faint erythema on her trunk, but no other rash. The heart was normal, and in the lungs a few wheezing rhonchi only were heard. No typhus spots appeared during the course of the illness. The crisis occurred on the eleventh day of illness, but the child did not rally, and the temperature fluctuated between 99° F., and 102.8° F., until 4th November when the patient died, that being the seventeenth day of illness.

Post-mortem examination revealed small patches of pneumonic consolidation at the upper part of the lower lobe of the left lung, with smaller masses scattered throughout the upper lobe. The heart muscle was pale, and the liver markedly fatty. The other organs were apparently normal.

Blood counts were commenced in this case on the eighth day of illness, and continued until death. The chart shows a fairly steady rise in the leucocytes up till the eleventh day of illness, then a fall of several thousands, a period of 24 hours, during which there was little change, and finally coincidently with the crisis, a steady rise to over 12,000, at which they remained practically stationary until death. This chart cannot be considered typical, as the lung

FATAL CASES Contd.

complication must have, to a certain extent, influenced the leucocytosis. The rise in the number of leucocytes during the crisis is peculiar, and in nearly every other case examined, the reverse was found, notwithstanding the complications.

Sputum not examined for diplococcus pneumon.

[illegible]	[illegible]	[illegible]	[illegible]		
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	6,700
30	11	[illegible]	[illegible]	[illegible]	10,600
31	12	100.	101.4	5,400	4,000
Nov. 1	13	101.8	101.4	3,800	6,600
2	14	98.6	100.6	13,300	12,000
3	15	100.4	101	8,400	
5	17	[illegible]	[illegible]		12,600

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CASE NO. 2. M. A. (aet. $1\frac{6}{12}$) admitted to hospital on first day of illness. Died on the seventeenth day of illness.

Date Oct.	Day of Illness	Temperatures M	Temperatures E	Total No. of Leucocytes M	Total No. of Leucocytes E
27	8	101.6°f	102.2°f		5,000
28	9	102.6	101.2		
29	10	102.	102.4	2,400	6,700
30	11	99.8	100.8	3,200	10,600
31	12	100.	101.6	3,600	4,000
Nov. 1	13	101.8	101.4	3,800	6,600
2	14	98.6	100.6	12,300	12,000
3	15	100.4	101	8,400	
5	17	99.	101		12,600

EXPLANATION OF CHART

Leucocytes	in Black
Temperature	In Red

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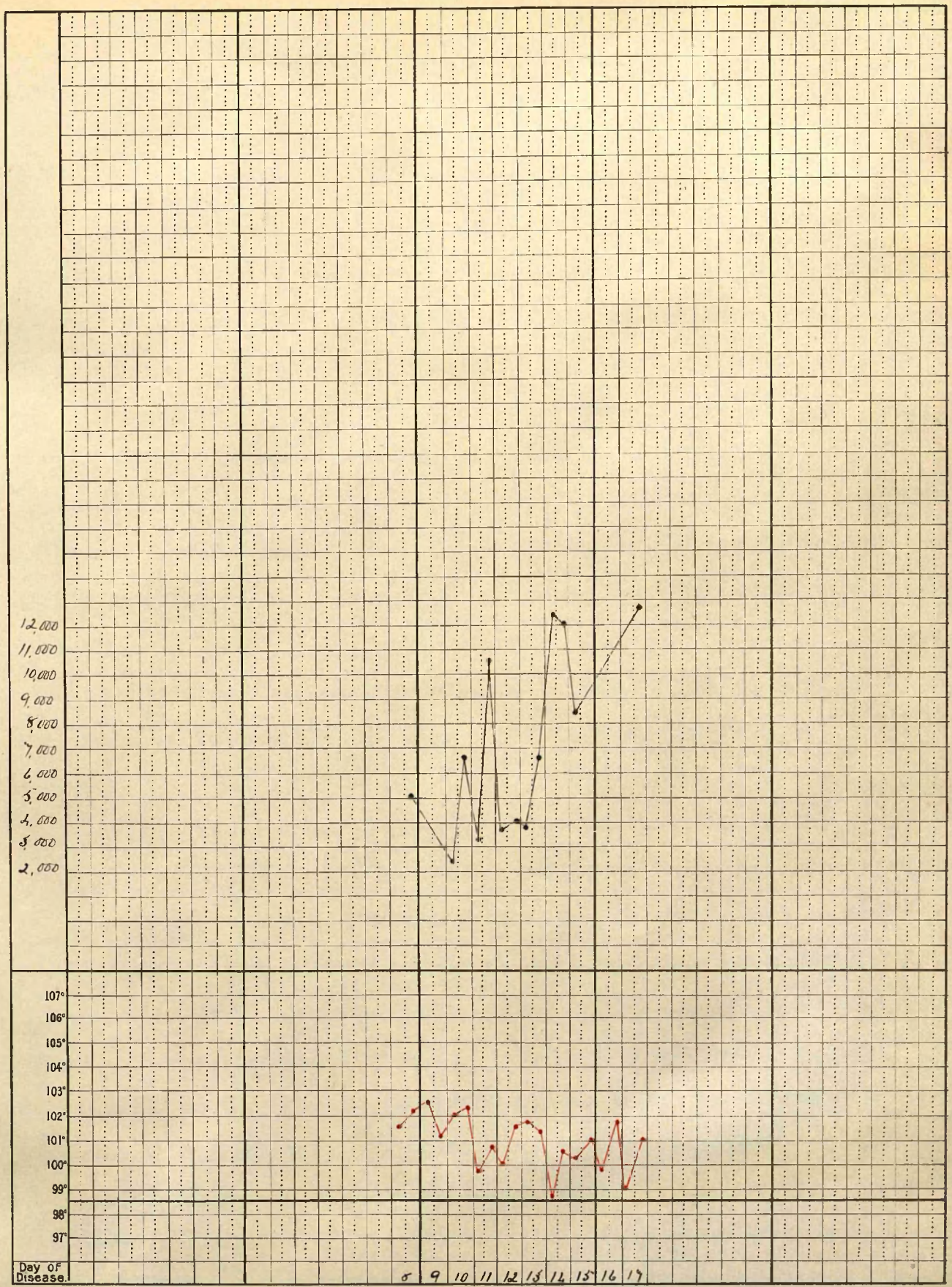
Chart II.


12,000
11,000
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7,000
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5,000
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107°
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99°
98°
97°
Day of Disease.
8
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16
17

FATAL CASES Contd.

CASE 3. Theresa A., aet. 3, another daughter of the first patient, was admitted from the reception house on 24th October 1902.

Her temperature had risen on the previous night to 99.6° F., and, on admission to hospital, it had reached 103.6° F., pulse rate 136, and respirations 44 per minute. The heart and lungs were normal. The patient looked very ill, and became gradually worse.

On 27th October (fifth day of illness), a typical typhus rash appeared on the thighs, developing rapidly over the body during this and the following days. From this time she gradually sank, and died on the evening of 6th November, that being her fourteenth day of illness.

Post-mortem examination revealed pallor of the cardiac muscle, hyperemia of both lungs, a fatty liver, and an enlarged hyperemic spleen.

In this case, a marked and progressive increase in the leucocytes towards the crisis was noted, and is well shown in the accompanying chart. It will be seen also from the chart that it was the polymorpho-nuclear variety mainly which contributed towards the increase, that there were no eosinophiles, and that the red corpuscles, which showed a gradual diminution towards the eleventh day, rose numerically about the time when the crisis might have been expected. This was a typical case of typhus without complications, dying about the period of crisis, and it is a noteworthy and interesting fact that examination of the fresh blood, immediately before death, showed degeneration and fragmentation of the red blood corpuscles.

CASE NO. 3. T. A. (aet. 3) admitted to hospital on second day of illness. Died on the fourteenth day of illness.

Date Oct.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono Nuclear Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
26	4	103.2°f	105°f						3,100
27	5	103.	105.					4,800	3,600
28	6	103.2	104	5,500,000				3,600	2,000
29	7	104.	104.6	4,400,000				3,600	4,800
30	8	102.	104.2	3,900,000	64.9	21.6	13.5	6,400	7,000
31	9	103.	104.6	4,200,000					
Nov. 1	10	102.4	104.4	3,840,000	75.9	15.5	8.6	7,000	9,400
2	11	103.2	104.2	3,760,000				9,400	6,600
3	12	103.4	104.	6,100,000	85.7	8.5	5.8	13,600	14,000
4	13	105.	105.8	5,905,000				7,400	15,400
5	14	105.4	105.4	5,870,000	81.5	11.3	7.2	12,000	13,200

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

26	4	103.2°f	105°f						3,100
27	5	103.	105.					4,800	3,600
28	6	103.2	104.					3,600	2,000
29	7	104.	104.6					3,600	4,800
30	8	102.	104.2		4,151	1,382	864	6,400	7,000
31	9	103.	104.6						
Nov. 1	10	102.4	104.4		5,313	1,085	602	7,000	9,400
2	11	103.2	104.2					9,400	6,600
3	12	103.4	104.		8,056	799	545	13,600	14,000
4	13	105.	105.8					7,400	15,400
5	14	105.4	105.4		9,780	1,356	964	12,000	13,200

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Temperature Chart	in Red

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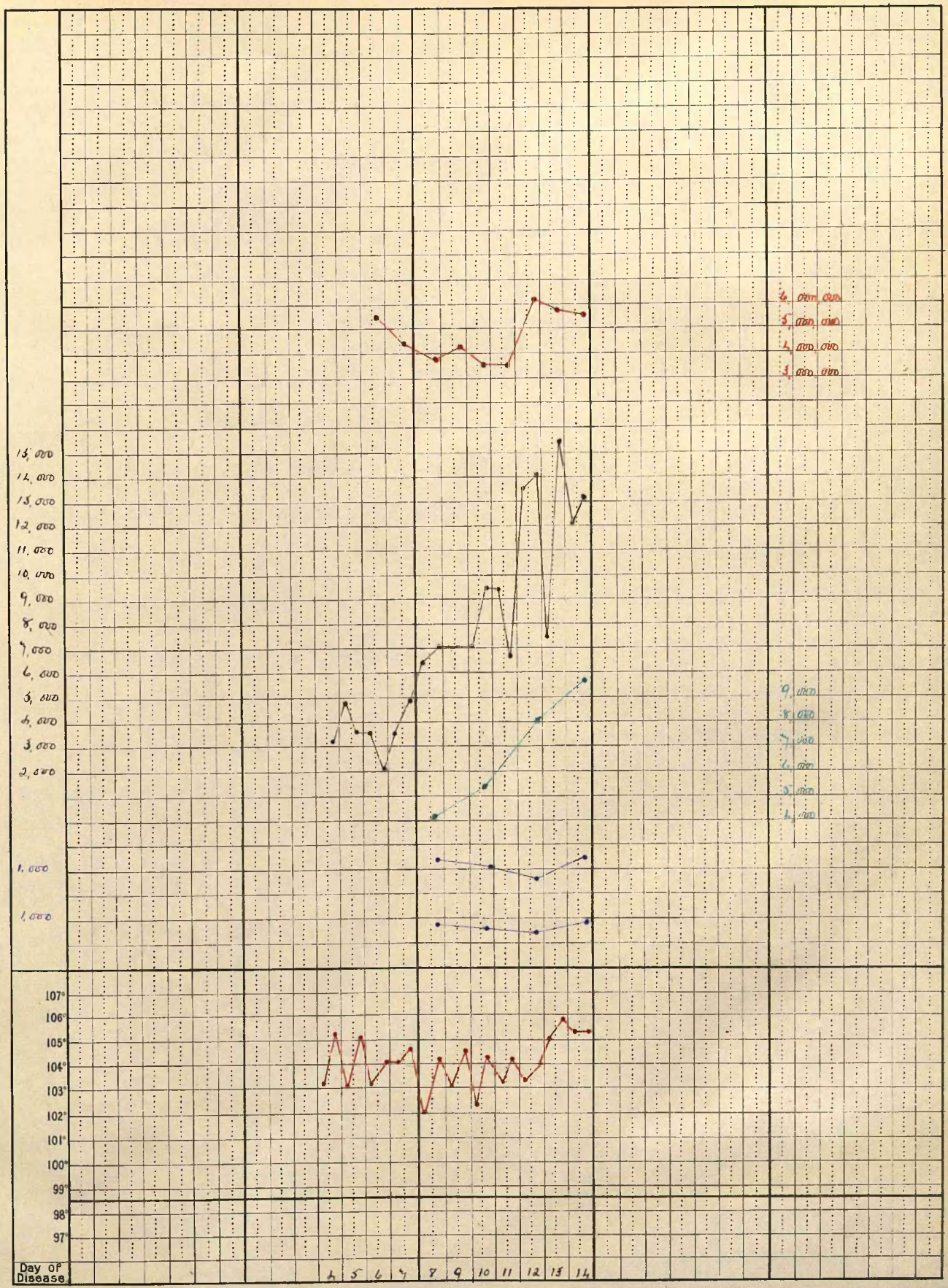
Chart III.


107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
Day of Disease
4 5 6 7 8 9 10 11 12 13 14

FATAL CASES Contd.

CASE 4. Mrs. S., aet. 33, was admitted to hospital on 3rd November 1902, with a history of having been sick for about ten days, and delirious for two. She was extremely ill, and had a profuse fixed typhus rash over the body, with patches of subcutaneous hemorrhage on the buttocks and back of the neck.

Her temperature was 104.8° F., pulse rate 136, and respirations 32 per minute. The patient gradually became worse, and died on the evening of her fifteenth day of illness, the day following the crisis

The accompanying chart shows no leucocytosis whatever, the corpuscles ranging within normal limits during the short period of the patient's residence in hospital. This is possibly due to the fact that the patient was so saturated with the poison of the fever that there was no reaction until immediately before death, when a slight ante-mortem rise occurred.

Here it will be again noted that there were no eosinophiles, and that the polymorpho-nuclear elements were the principal participators in the rise and fall of the leucocytes.

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CASE NO. 4. Mrs. S. (aet. 33) admitted to hospital on ninth day of illness. Died on the fifteenth day of illness.

Date Nov.	Day of Illness	Temperatures M	E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono Nuclear Cells per cent.	Total No. of Leucocytes M	E
3	9	104.8°f	105°f	3,335,000	88.2	11.1	7		2,900
4	10	104	105	3,260,000				7,200	6,600
5	11	103.8	103.8	4,260,000	86	13.5	5	8,200	5,200
6	12	103.8	102.6	5,400,000	82.2	12.9	4.9	4,400	7,400
7	13	103	102.6	4,170,000	81.2	16.2	2.6	4,400	5,800
8	14	102.4	101.6	4,070,000	84	13.4	2.6	5,600	6,600
9	15	98.4	98.6	4,650,000	84	5	11	8,400	

The following are the absolute numbers of the different varieties of Leucocytes calculated from the above

3	9	104.8°f	105°f		2,558	322	20		2,900
4	10	104	105					7,200	6,600
5	11	103.8	103.8		7,052	1,107	41	8,200	5,200
6	12	103.8	102.6		3,617	567	216	4,400	7,400
7	13	103	102.6		3,573	713	114	4,400	5,800
8	14	102.4	101.6		4,704	750	146	5,600	6,600
9	15	98.4	98.6		7,056	420	924	8,400	

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Temperature Chart	in Red

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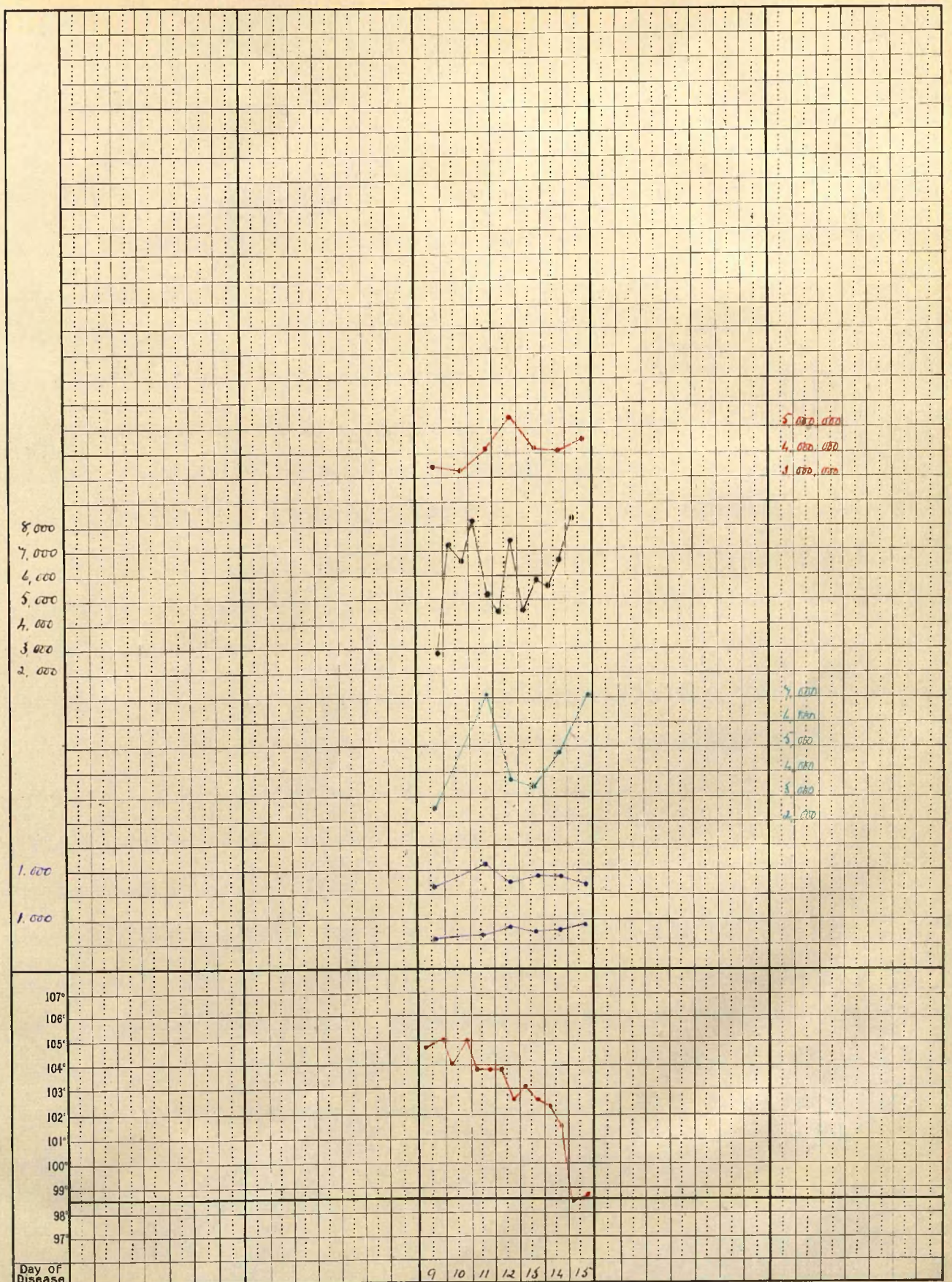
Chart IV.


8,000
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107°
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Day of Disease.
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15

FATAL CASES Contd.

CASE 5. Nellie S., aet. 9, a daughter of the last patient, is a case of great interest. She was admitted on 9th November 1902 from the reception house. Her temperature had risen slightly on the previous night (8th), and on admission to hospital it was 99.8° F., pulse rate 100, and respirations 24 per minute.

This case is interesting from the fact that, during the course of her illness, she developed an acute gangrenous condition with destruction of the upper part of the right lung, a complication which apparently but little influenced the number of her leucocytes, and also from the fact that she came under observation on her second day of illness.

When admitted to hospital she did not seem very ill, and was a well nourished and healthy looking child. Examination of her chest revealed nothing abnormal. The typical typhus eruption appeared on 15th November, that being her eighth day of illness if the onset is calculated from the first slight rise in temperature, or her fifth day of illness if the onset be estimated from the sudden rise of temperature to 101.4° F., on 11th November. She gradually became worse, and signs of consolidation were detected in her right lung on 19th November; this rapidly broke down, and signs of cavity were soon apparent. Rapidly becoming worse, she died on 29th November about midnight.

Post-mortem examination revealed consolidation of the upper half of the superior lobe of the right lung, with a cavity in the centre

FATAL CASES Contd.

of the solid portion about the size of a walnut. The diseased lung emitted a gangrenous odour. The spleen was enlarged and hyperemic. The left lung and other organs were normal.

An examination of the accompanying chart reveals certain points of interest, viz., great variations in the morning and evening leucocyte counts, with a steady increase towards the crisis, which occurred on 19th November (twelfth day of illness), thereafter a slight variation for two or three days, followed by a steady fall to normal, and again a striking ante-mortem rise immediately before death. Once more it will be observed there were no eosinophiles, and that the polymorpho-nuclear leucocytes were the cells which varied most. The red corpuscles also participated in the rise towards the crisis, but fell immediately after, rising again, however, before death.

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CASE NO. 5. N. S. (aet. 9) admitted to hospital on the first day of illness. Died on the twenty-first day of illness.

Date Nov.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono Nuclear Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
10	2	99,2°f	99.2°f	5,520,000	83	12	5	10,200	12,200
								11,200	12,600
11	3	98.6	101.4	5,190,000					
12	4	101	102.2	4,240,000	85	10	5	17,800	11,800
13	5	102.4	103.4	4,980,000	90	7	3	8,000	11,000
14	6	102.4	104.2	4,120,000	84.8	11.2	4	18,000	13,200
15	7	103	103.8	4,770,000	82	11.5	6.5	13,400	7,800
16	8	102.6	104	5,000,000	82	10	8	20,400	10,000
17	9	102.4	103.4	5,001,000	88	7	5	13,000	11,000
18	10	102.2	104	6,200,000	89	6	5	12,800	26,400
19	11	103	104	7,090,000	80	12.5	7.5	27.200	16,000
20	12	99.6	102.6	7,000,000	80	13	7	27,600	20,000
21	13	101.6	103.8	7,200,000	85.5	9.5	5	26,800	27,800
22	14	101.8	103.2	4,750,000	84.5	9	6.5	24,400	14,200
23	15	101.4	104.8	4,300,000	85	9	6	16,000	15,000
24	16	101.4	104.2	4,150,000	86.5	6	7.5	15,800	12,000
25	17	102.4	104.8	5,300,000	81	9	10	10,200	14,000
26	18	102.4	104.4	5,000,000	82	9	9	7,200	6,400
29	21	101.4	103.8	6,500,000	87	5	8	23,200	20,800

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above.

10	2	99.2°f	99.2°f	8,446	1,222	510	10,200	12,800
							11,200	12,600
11	3	98.6	101.4					
12	4	101	102.2	15,130	1,780	89	17,800	11,800
13	5	102.4	103.4	7,200	560	240	8,000	11,000
14	6	102.4	104.2	15,264	2,016	720	18,000	13,200
15	7	103	103.8	10,988	1,541	871	13,400	7,800
16	8	102.6	104	16,728	2,040	1,632	20,400	10,000
17	9	102.4	103.4	11,440	910	650	13,000	11,000
18	10	102.2	104	11,392	768	640	12,800	26,400
19	11	103	104	21,760	3,400	2,040	27,200	16,000
20	12	99.6	102.6	22,080	3,588	1,932	27,600	20,000
21	13	101.6	103.8	22,914	2,456	1,340	26,800	27,800
22	14	101.8	103.2	20,618	2,196	1,586	24,400	14,200
23	15	101.4	104.8	13,600	1,440	960	16,000	15,000
24	16	101.4	104.2	13.667	948	1,185	15,800	12,000
25	17	102.4	104.8	8,262	918	1,020	10,200	14,000
26	18	102.4	104.4	5,904	648	648	7,200	6,400
29	21	101.4	103.8	20,184	1,160	1,856	23,200	20,800

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Temperature Chart	in Red

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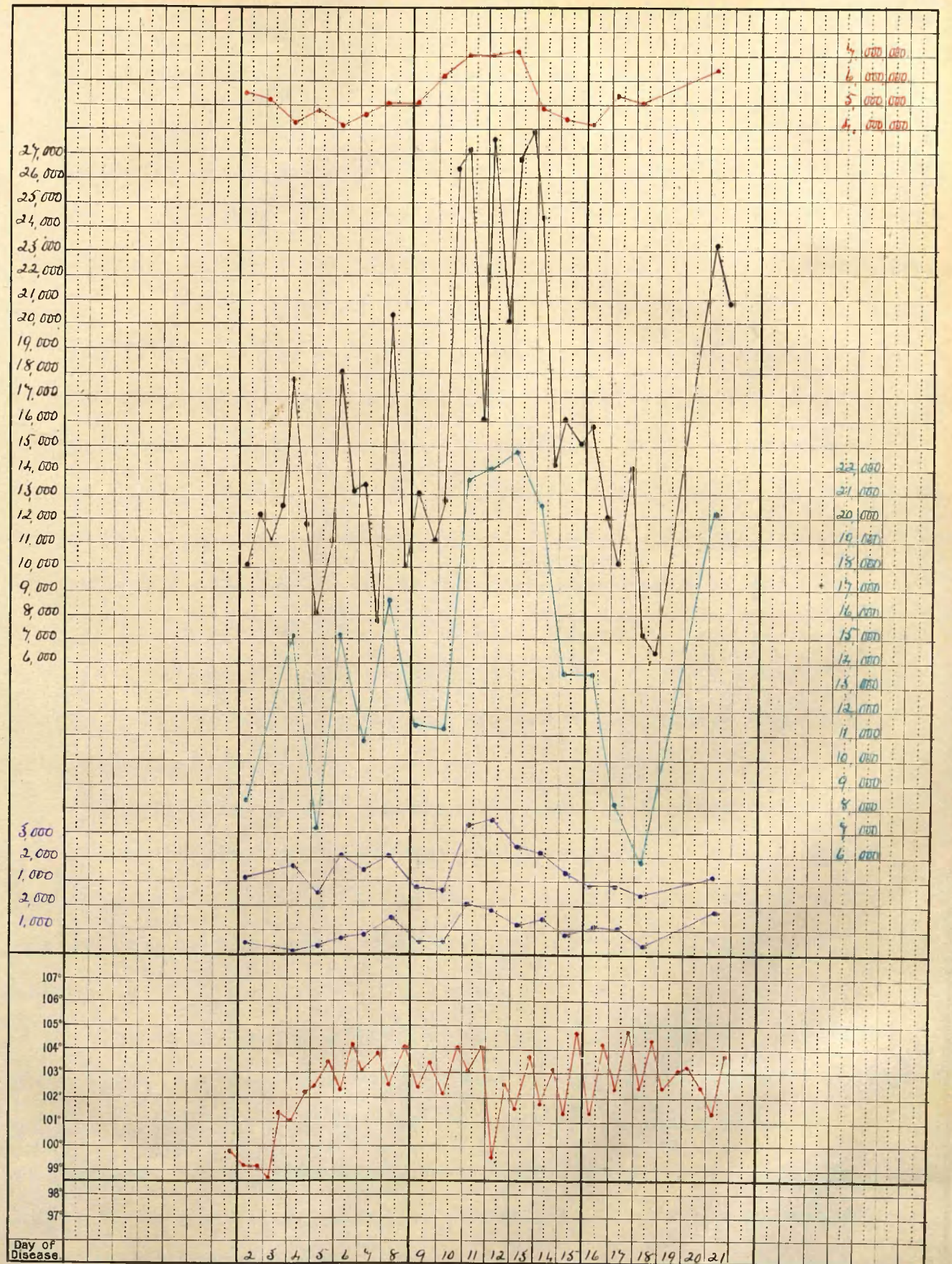
Chart V.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FATAL CASES Contd.

CASE 6. Mrs. E., aet. 56, admitted on 13th November 1902 from the reception house. This patient was a "contact", and her temperature, which on the night previous to admission (12th) had risen to 100.4° F., was found to be 103° F. on the afternoon of the 13th.

On admission to hospital her temperature was 98.4° F., pulse rate 92, and respirations 24 per minute. Patient looked and felt absolutely well, and on physical examination nothing abnormal was detected in any of the organs. On 16th November mottling of the skin was noticed, and on the following day the typical typhus eruption appeared. She became much worse on the 21st, gradually sank, and died on 23rd November, her twelfth day of illness.

Post-mortem examination disclosed a flabby pale heart, an enlarged and diffluent spleen, and extensive sub-mucous hemorrhages in the intestinal tract.

In this case it will be observed there was a gradual rise in the number of leucocytes as the crisis approached, with a more rapid increase on the morning of the day preceding death, and a very striking decline in numbers in the evening. The ante-mortem rise was very slight.

In this as in the preceding cases, no eosinophile corpuscles were found, and the leucocytosis was due mainly to increase in the polymorpho-nuclear cells. The presence of an increase in the number of red corpuscles throughout, over 8,000,000 per c.m., is very striking. These numbers appeared so remarkable that repeated estimates were made to verify them.

CASE NO. 6. Mrs. E. (aet. 56) admitted to hospital on second day of illness. Died on the twelfth day of illness.

Date Nov.	Day of Illness	Temperatures M	E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono Nuclear Cells per cent.	Total No. of Leucocytes M	E
14	3	100°f	102°f	5,310,000	74.8	18.4	6.8	13,000	15,800
15	4	101.4	101	8,830,000	84.3	13.6	2.3	8,600	9,800
16	5	102.4	104.2	8,070,000	81.3	13.7	5	9,000	16,000
17	6	104.4	101.4	8,260,000	79.3	12	8.7	13,400	12,400
18	7	103	104.2		84.3	5.7	10	13,200	18,600
19	8	102.2	103.2	7,800,000	86.9	6.7	6.4	12,800	17,000
20	9	103.2	102.6	8,500,000	90	5.2	4.8	36,400	18,000
21	10	104	103.2	7,070,000	85.1	5.2	9.6	18,600	28,600
22	11	102.2	103.2		78.1	11.7	10.1	54,400	23,600
23	12	104.4	105	8,700,000	90	4	6	23,600	26,400

The following are the Absolute Numbers of the different varieties of Leucocytes caloulated from the above

14	3	100°f	102°f	9,724	2,492	884	13,000	15,800
15	4	101.4	101	7,250	1,170	180	8,600	9,800
16	5	102.4	104.2	7,318	1,232	450	9,000	16,000
17	6	104.4	101.4	10,626	1,166	1,608	13,400	12,400
18	7	103	104.2	11,128	752	1,320	13,200	18,600
19	8	102.2	103.2	11,123	858	819	12,800	17,000
20	9	103.2	102.6	32,760	1,893	1,747	36,400	18,000
21	10	104	103.2	15,829	967	1,804	18,600	28,600
22	11	102.2	103.2	42,486	6,419	5,495	54,400	23,600
23	12	104.4	105	21,240	944	1,416	23,600	26,400

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Temperature Chart	in Red

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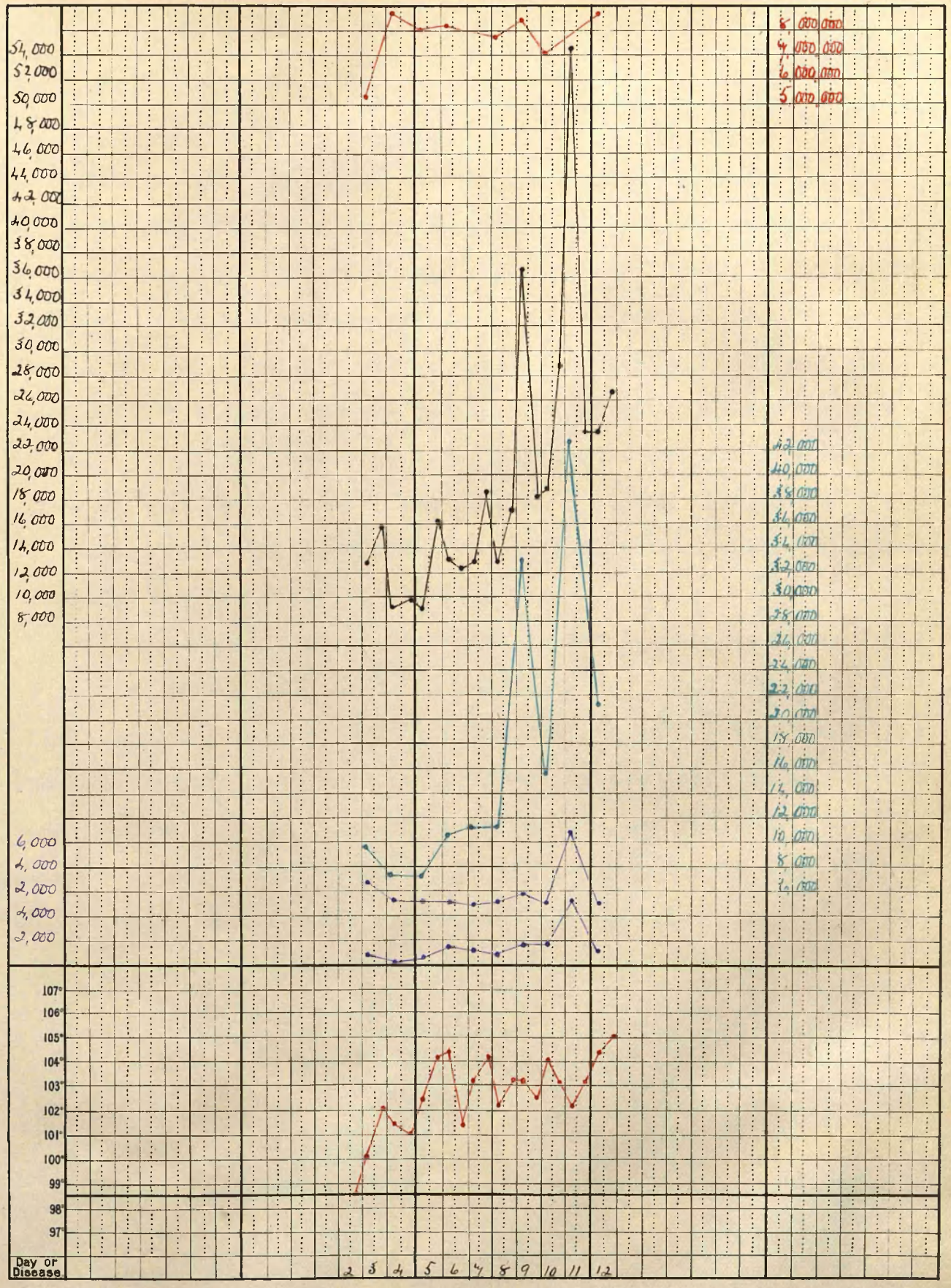
Chart VI.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Day of Disease
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FATAL CASES Contd.

CASE 7. Mrs. G., aet. 36, was admitted to hospital on 19th November from the reception house, to which she had been admitted after having been ill in her own house for two or three days. Her temperature on the night previous to admission was 100.6° F., and on the day of admission 100.8° F., her pulse rate was 112, and respirations 24 per minute. On the day after admission to hospital, the typical typhus eruption appeared. Physical examination of her chest revealed nothing abnormal. She gradually became weaker, and died on 1st December, her sixteenth day of illness, shortly after the temperature had dropped to near normal.

The same conditions with regard to the leucocytes prevail here as in the other fatal cases - a gradual rise in the number as the crisis approached, a marked rise immediately before or at the crisis, and a fall during or immediately after, with a distinct ante-mortem rise. Again, no eosinophiles were present, and the polymorpho-nuclear corpuscles predominated. It will be noted also that the number of red corpuscles was fairly high throughout.

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CASE NO. 7. Mrs. G. (aet. 36) admitted to hospital on fourth day of illness. Died on the fifteenth day of illness.

Date Nov.	Day of Illness	Temperatures M	E	Red Cells	Polymorpho Nuclear Cells per cent	Lymphocytes per cent.	Large Mono-Nuclear Cells per cent.	Total No. of Leucocytes M	E
20	5	99.8°f	103.2°f	4,670,000	88	8.0	4	6,200	
21	6	103.2	104.4	6,050,000	89.7	5.8	4.5	8,000	5,400
22	7	101.8	104.4	5,500,000	89.4	4.7	5.9	6,800	6,800
23	8	103	105	5,650,000	89.9	4.5	5.6	4,000	8,800
24	9	102.2	104.2	8,400,000	82.8	1.4	5.8	10,200	11,800
25	10	103.4	104.4	6,850,000	93		7	17,400	15,200
26	11	104	104.2	6,450,000	93		7	15,800	16,200
27	12	103	101.2	5,700,000	90.2	1.2	8.6	20,000	35,000
28	13	101.4	102.2	7,950,000	90.1	2.7	7.2	32,000	31,000
29	14	100.2	100.2	7,050,000	92.9	.6	6.5	17,000	13,700
30	15	103.2	104	6,900,000	92.8	.4	6.8	23,800	25,800

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

20	5	99.8°f	103.2°f		5,456	496	248	6,200	
21	6	103.2	104.4		7,176	464	360	8,000	5,400
22	7	101.8	104.4		6,079	320	401	6,800	6,800
23	8	103	105		5,596	180	224	4,000	8,800
24	9	102.2	104.2		9,465	143	592	10,200	11,800
25	10	103.4	104.4		16,182		1,218	17,400	15,200
26	11	104	104.2		14,694		1,106	15,800	16,200
27	12	103	101.2		18,040	240	1,720	20,000	35,000
28	13	101.4	102.2		28,832	864	2,340	32,000	31,000
29	14	100.2	100.2		15,793	102	1,105	17,000	13,700
30	15	103.2	104		23,087	95	1,618	23,800	25,800

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Temperature Chart	in Red

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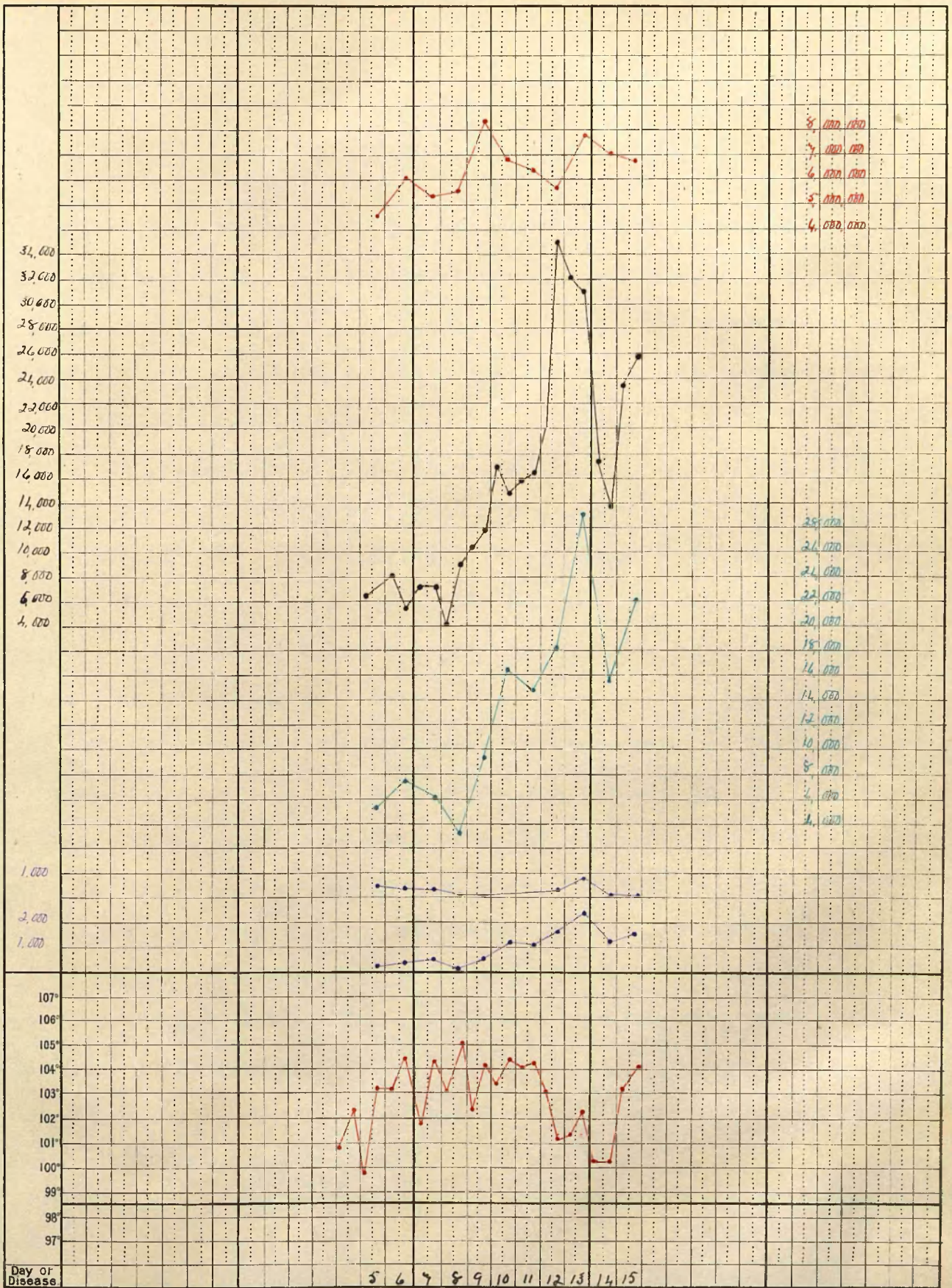
Chart VII.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Day of Disease
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FATAL CASES Contd.

CASE 8. Thomas B., aet. 45, was admitted to hospital on 28th December 1902. No history was obtainable. His temperature on admission was 103.2° F., pulse rate 124, and respirations 32 per minute.

He was very ill and delirious, and his skin presented a definite fixed typhus eruption over trunk and limbs. He died twenty hours after admission to hospital.

Post-mortem examination disclosed hypertrophy of the left ventricle, with thickening of the aortic and mitral valves, adherent pleurae, and calcareous nodules in both lungs, with edema of both bases. The spleen was enlarged and diffluent. The kidneys were engorged, and there were hemorrhages into the sub-mucous coat along the whole intestinal tract.

Two observations on the leucocytes were made in this case, one in the morning and one in the evening of the day on which he was admitted. Both, as will be seen from the chart, showed the existence of a marked leucocytosis, and both were verified by other observers.

Here again the polymorpho-nuclear cells were most abundant, and no eosinophiles were found, a correspondence being thus shown with the other fatal cases. The red cells were numerous, over 8,000,000 per c.m. being present.

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CASE NO. 8. T. B. (aet. 45) admitted to hospital on the ninth day of illenss. Died on the tenth day of illness

Date Dec.	Day of Illness	Temperatures M	E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono Nuclear Cells per cent.	Total No. of Leucocytes M	E
26	10	102.4°f	101.8°f	8,300,000	89.5	5.2	5.3	38,000 12 noon	29,000 5 p.m.

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

26	10	102.4°f	101.8°f		34,010	1,976	2,014	38,000	29,000

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Temperature Chart	in Red

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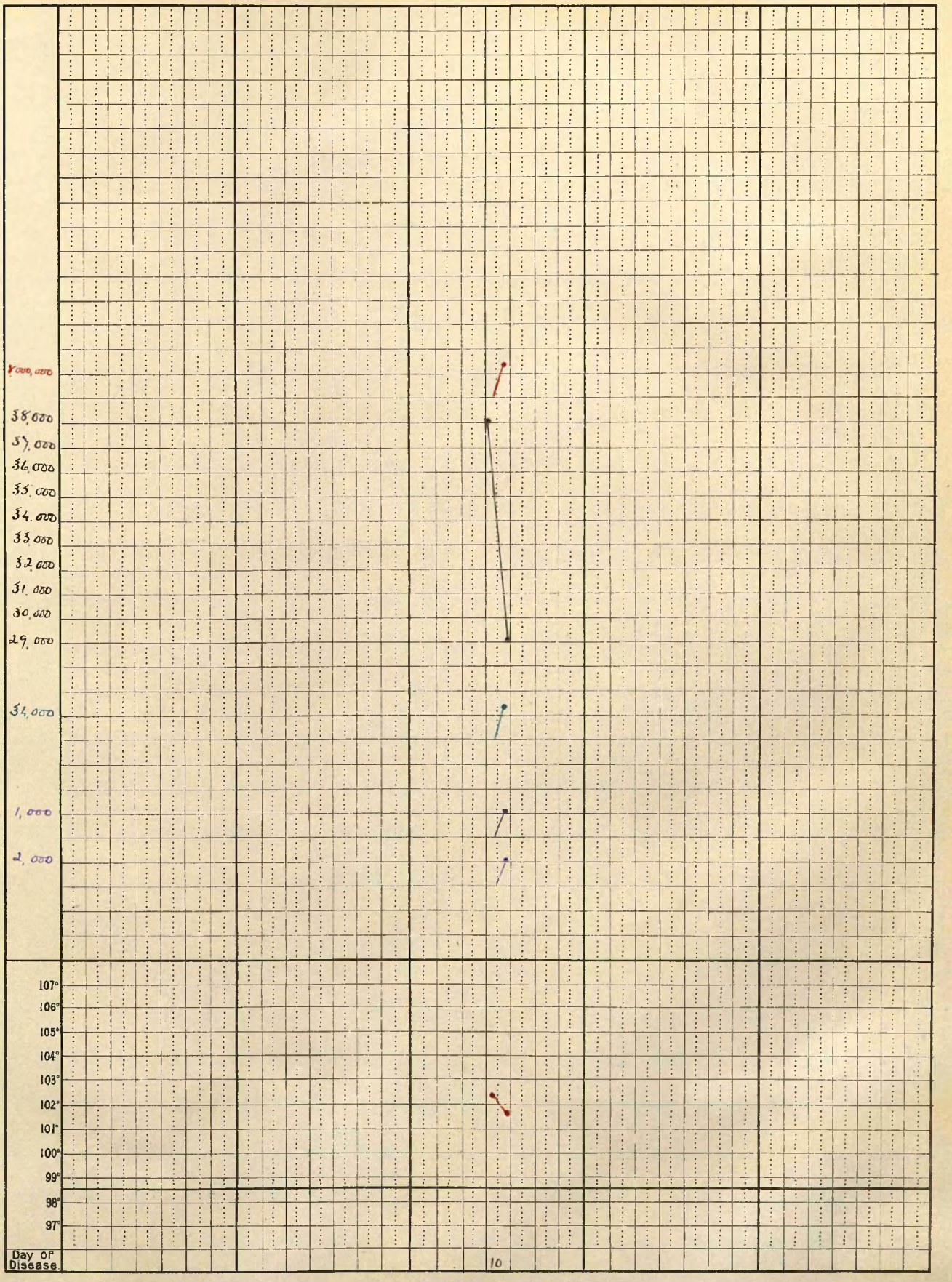
Chart VIII.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Day of Disease
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FATAL CASES Contd.

CASE 9. Matilda D., aet. 15, is the last of the series of fatal cases. This patient was admitted to hospital on 11th March 1903, her fourth day of illness. Her temperature was 104.2° F., pulse rate 120, and respirations 32 per minute. She was very ill, and there was present an eruption of early typhus spots of a somewhat deep red colour on the chest, abdomen, back, arms, buttocks, and thighs.

On 16th March (ninth day of illness) the rash was becoming fixed. A high pyrexia was present with practically no remission until 24th March, on which day the crisis occurred, the temperature falling from 105.4° F. to 100.8° F.; it rose again, however, almost immediately, and continued to rise during the night and following day, until it reached 107.2° F. just before death on the afternoon of 25th March. During the last three or four days of her illness, dulness at the bases of both lungs behind, with fine crepitant râles, was detected, and this complication no doubt contributed greatly towards the fatal issue. Unfortunately no post-mortem examination was obtained.

The accompanying chart shows that, although there was a leucocytosis, it was not great. It corresponds with the other fatal cases, however, in so far as there was a fall in the number of leucocytes at the crisis, and in that no eosinophile corpuscles were found. This case also shows in a striking manner the great ante-mortem leucocyte rise which sometimes takes place, a phenomenon which suggests that possibly at this time only was there any decided reaction on the part

FATAL CASES Contd.

of the blood forming organs. The fact that the pneumonic process apparently gave rise to no increase in the leucocytes, also points to the absence of reaction. The red corpuscles showed no increase, and remained practically normal throughout the course of the disease.

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CASE NO. 9. M. D. (aet. 15) admitted to hospital on the fourth day of illness. Died on the eighteenth day of illness

Date Mar.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono Nuclear Cells per cent.	Total No. of Leucocytes
15	8	104°f	104.6°f	6,240,000	82	14	4	10,000
16	9	104.2	104.6		83	13	4	8,800
17	10	104.4	104.6	6,850,000	84	12	4	14,000
18	11	104.4	104.6		82.5	14	3.5	14,800
19	12	104.2	104.4	5,550,000	78	17	5	15,200
20	13	103.4	104		81	15	4	12,000
21	14	104	104.4	6,200,000	79	17	4	11,400
22	15	103.6	104.6		79	16	5	10,000
23	16	105.4	104.4	5,070,000	75	18	7	15,000
24	17	100.8	102.2		81	14	5	6,000
25	18	104	107.2	6,000,000	81	14	5	45,000

The following are the absolute numbers of the different varieties of Leucocytes calculated from the above

15	8	104°f	104.6°f	8,200	1,400	400	10,000	
16	9	104.2	104.6	7,304	1,144	352	8,800	
17	10	104.4	104.6	11,760	1,680	560	14,000	
18	11	104.4	104.6	12,210	2,072	518	14,800	
19	12	104.2	104.4	11,856	2,580	760	15,200	
20	13	103.4	104	9,720	1,800	480	12,000	
21	14	104	104.4	9,006	1,938	456	11,400	
22	15	103.6	104.6	7,900	1,600	500	10,000	
23	16	105.4	104.4	11,250	2,700	1,050	15,000	
24	17	100.8	102.2	4,860	840	300	6,000	
25	18	104	107.2	36,450	6,300	2,250	45,000	

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	In Violet
Lymphocytes	in Violet
Temperature Chart	in Red

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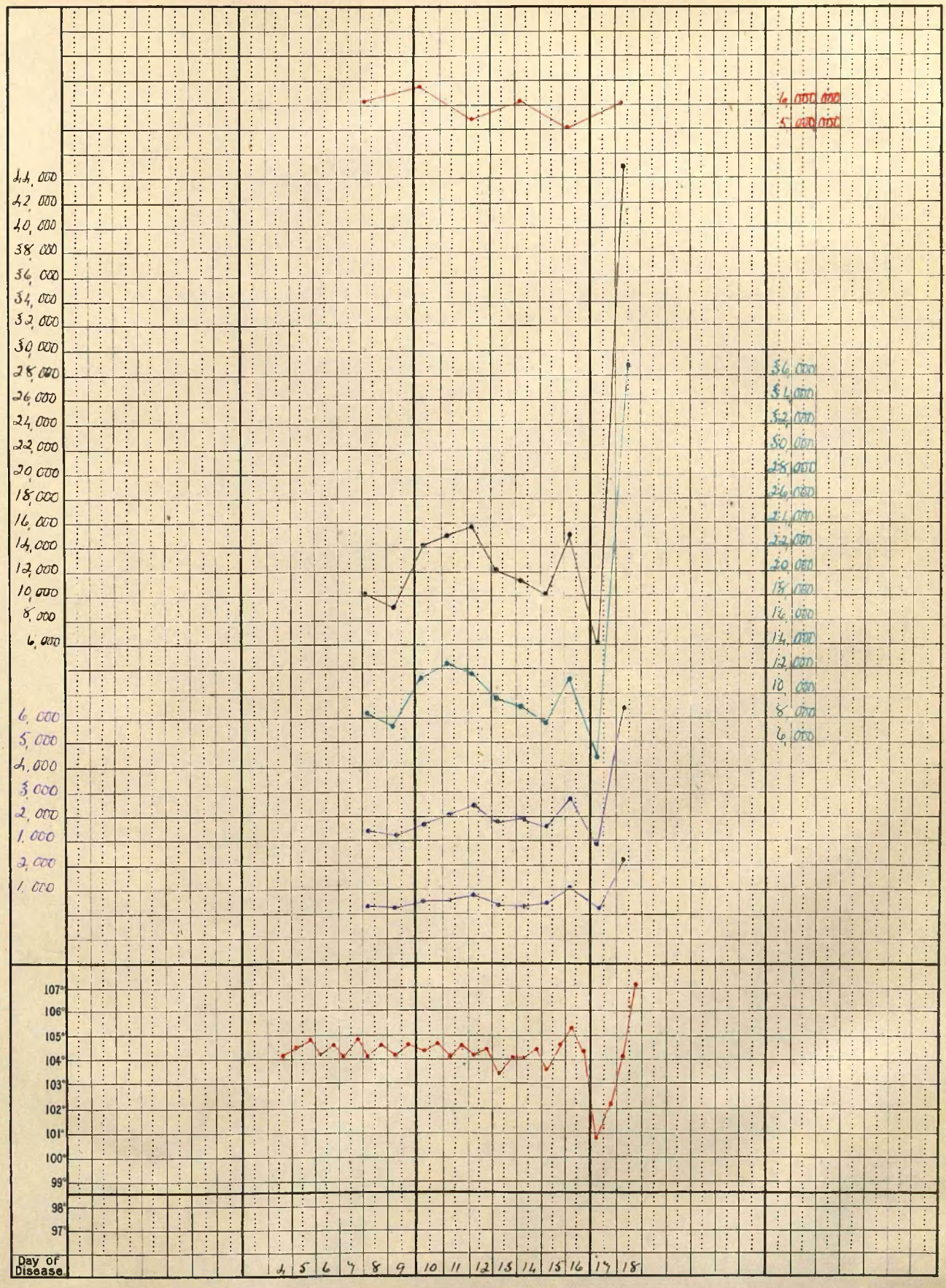
Chart IX.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Day of Disease
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FATAL CASES Contd.

To sum up briefly, it is to be observed that, in fatal cases, there is:-

1. A leucocytosis (except in cases where no reaction is manifested) increasing towards the crisis
2. A fall at, or immediately after the crisis, and in most cases an ante-mortem rise
3. Absence of eosinophile corpuscles
4. A relatively high proportion of red blood corpuscles.

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GROUP II - RECOVERIES

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CASE 1. Annie A., aet. 6, was admitted on 15th October 1902. Her temperature on admission was 101.4° F., pulse rate 116, and respirations 26 per minute. A few typhus spots were present on the back and thighs. The crisis occurred during the fourteenth and fifteenth days of illness, and patient's convalescence was uninterrupted.

This was one of the early cases admitted to hospital, and two leucocyte estimations only were made, but these showed that leucocytosis was present, and that a fall in the number of leucocytes was taking place coincidentally with the crisis.

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CASE NO. 1. A. A. (aet. 6) admitted to hospital on 12th day of illness.

Date Oct.	Day of Illness	Temperatures M	E	Leucocytes
16	13	101.4	103.8	16,000
17	14	100.6	101.8	10,000

EXPLANATION OF CHART

Leucocytes in Black

Temperature in Red

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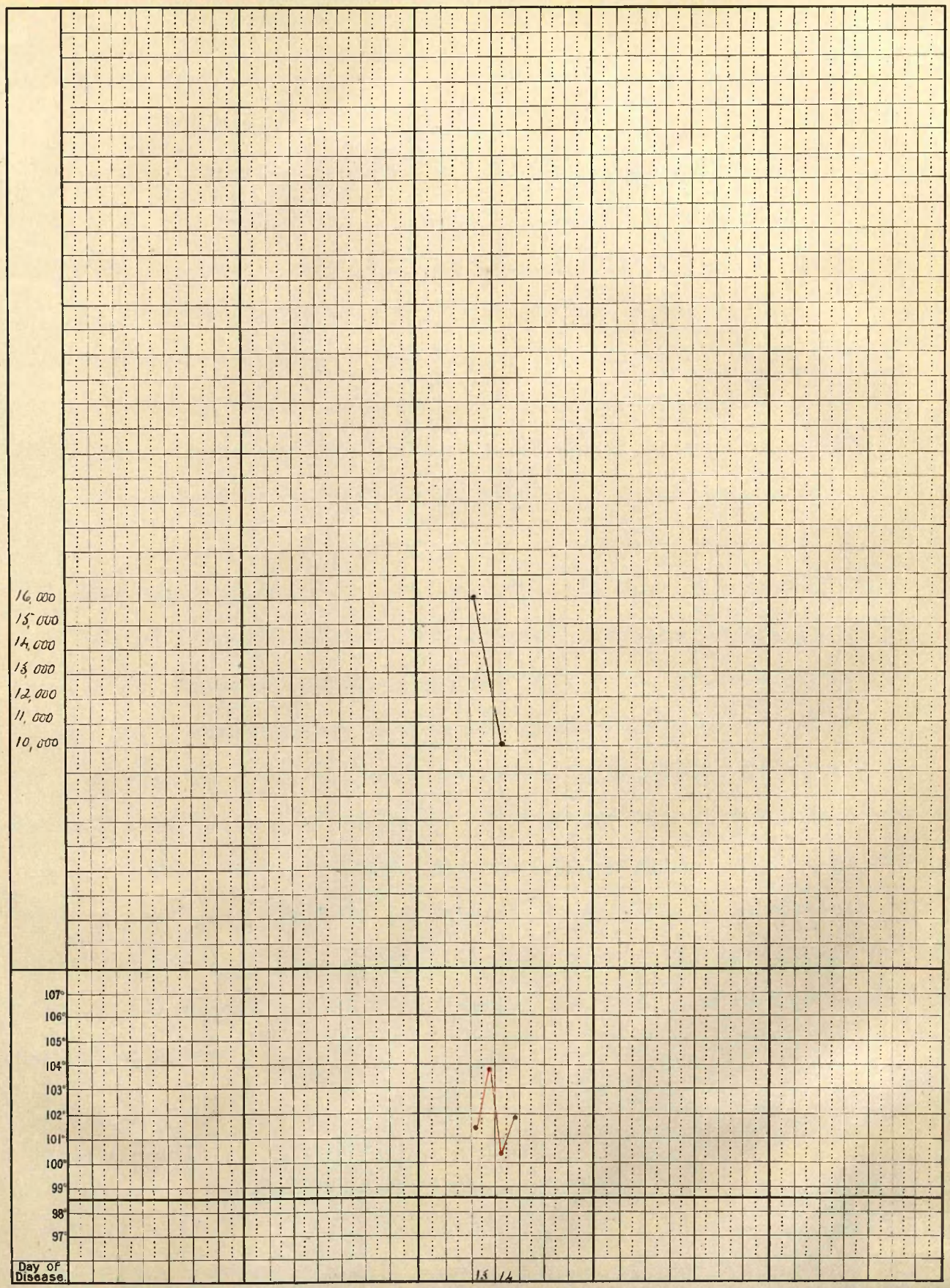
Chart I.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Day of Disease
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14

RECOVERIES Contd.

CASE 2. Francis A., aet. 4, was admitted on 27th October 1902, that being his second day of illness. His temperature on admission was 98.2° F., pulse rate 124, and respirations 36 per minute.

On 30th October (fifth day of illness), a typical typhus eruption appeared on the trunk and limbs. The disease ran its usual course, and the crisis occurred on the fourteenth day of illness, after which there was an uninterrupted convalescence, with the exception of a slight bronchitis which developed a few days after the crisis.

The chart of this case shows very well the interesting fact that just before the crisis there was a great increase in the number of leucocytes, and thereafter a decided fall. The secondary rise noted on the chart was possibly due to the bronchitis.

It will be observed that the polymorpho-nuclear cells mainly participated in the increase, but that there was also an increase in the large mono-nuclear forms, and that eosinophile corpuscles were present; this last variety of leucocyte, it will be remembered, was absent in all the fatal cases. The red corpuscles throughout were practically normal except just before the crisis, when there was a marked increase.

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CASE NO. 2. F. A. (aet. 4) admitted to hospital on second day of illness

Date Oct.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
27	2	98.2°f	99°f						7,800	6,800
28	3	101	103.2	4,400,000					4,600	4,000
29	4	101.4	101.2	5,100,000					9,200	6,700
30	5	99.6	103.8	5,000,000					5,800	5,200
31	6	103.8	104.2	5,280,000						
Nov. 1	7	102.4	105	4,640,000	52.5	33.5	14		4,600	7,000
2	8	102	102.6	3,336,000					7,200	9,000
3	9	103.8	103.8	4,008,000	70	22	7.5	.5	4,100	4,900
4	10	102.2	104.8	3,610,000					6,000	3,400
5	11	101.6	103	6,150,000	70	23	7		5,600	8,400
6	12	102	103.8	6,730,000					5,900	8,000
7	13	102	103	4,540.000	60	25	14	1	15,400	20,000
8	14	101	98.4	4,760,000	57.5	27.5	13	2	17,600	13,000
9	15	98	99	3,500,000	56	26	16	2	10,000	13,800
10	16	98.4	99	4,690,000	65	26	9		10,400	12,600
11	17	99.2	99	4,740,000					8,600	6,800
12	18	98	99	5,700,000					15,000	
13	19	97	98	5,700,000	65	27,75	7	.25	14,200	14,000
15	21	97.6	98.6	5,120,000	65	30	5		15,200	15,800
17	23	98	99	5,200,000					12,800	12,000
Dec. 10	46	98	98.8	4,900,000	75.5	20	4	.5	7,900	7,700
13	49	98	98.6	4,500,000	70	25	4	.1	5,000	4,000

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

27	2	98.2°f	99°f						7,800	6,800
28	3	101	103.2						4,600	4,000
29	4	101.4	101.2						9,200	6,700
30	5	99.6	103.8						5,800	5,200
31	6	103.8	104.2							
Nov. 1	7	102.4	105	2,415	1,541		644		4,600	7,000
2	8	102	102.6						7,200	9,000
3	9	103.8	103.8	2,870	902		308	20	4,100	4,900
4	10	102.2	104.8						6,000	3,400
5	11	101.6	103	3,920	1,228		392		5,600	8,400
6	12	102	103.8						5,900	8,000
7	13	102	103	9,240	3,850		2,156	154	15,400	20,000
8	14	101	98.4	10,120	4,840		2,288	352	17,600	13,000
9	15	98	99	5,600	2,600		1,600	200	10,000	13,800
10	16	98.4	99	6,760	2,704		936		10,400	12,600
11	17	99.2	99						8,600	6,800
12	18	98	99						15,000	
13	19	97	98	9,230	3,941		994	35	14,200	14,000
15	21	97.6	98.6	9,880	4,560		760		15,200	15,800
17	23	98	99						12,800	12,000
Dec. 10	44	98	98.2	5,964	1,580		316	40	7,900	7,700
13	47	98.4	98.2	3,500	1,250		200	50	5,000	4,000

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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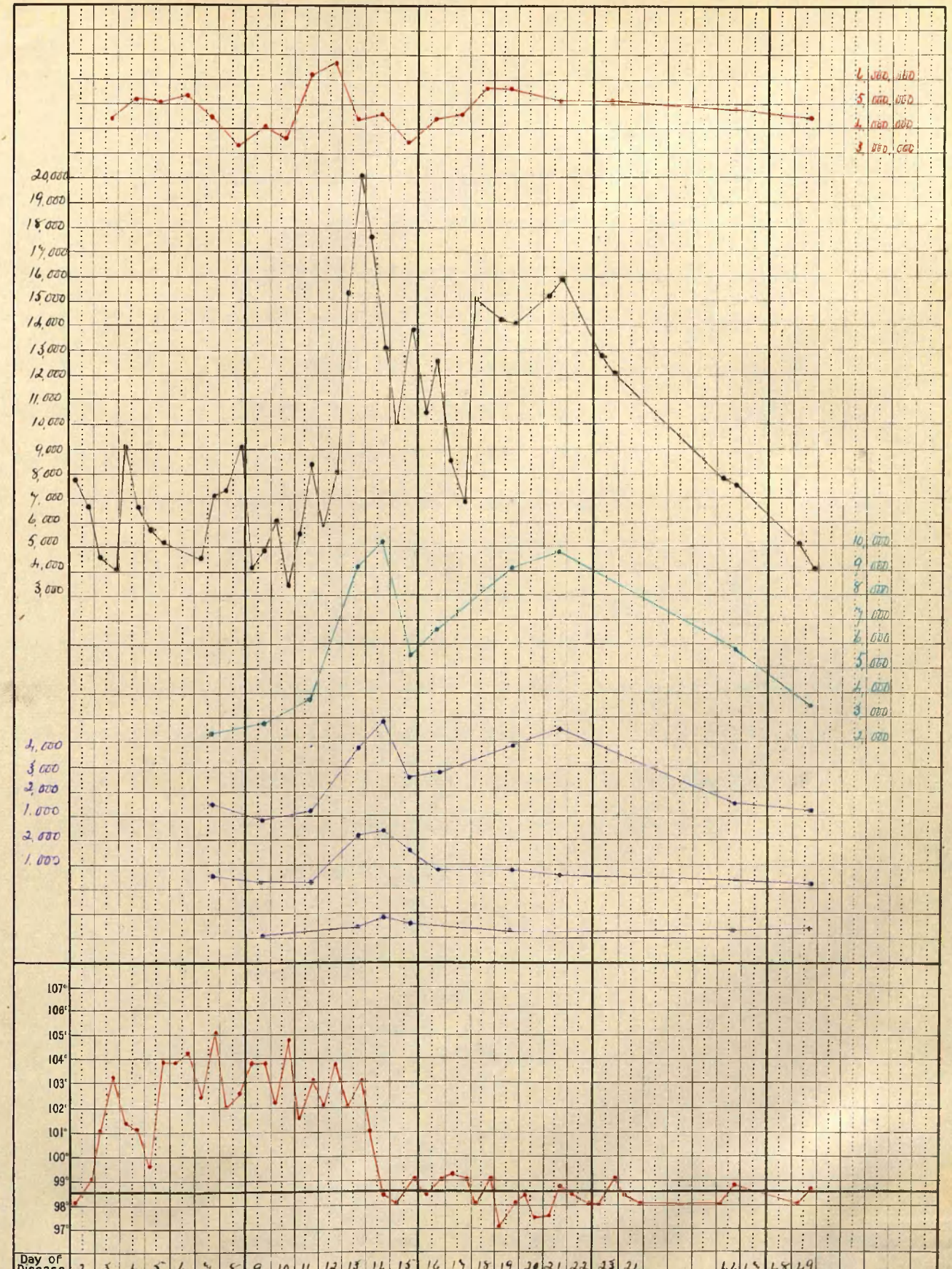
Chart II.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RECOVERIES Contd.

CASE 3. Mary S., aet. 13, was admitted on 3rd November 1902, her fifth day of illness. Her temperature on admission was 103.8° F, pulse rate 116, and respirations 24 per minute. A distinct typhus eruption was present over the whole of the body. The heart and lungs were normal. The disease ran a moderately mild course, and the crisis occurred during the fourteenth and fifteenth days of illness, after which convalescence was uninterrupted.

The usual features will be noticed in the chart of this case - a fluctuating leucocytosis until just before the crisis, when a marked rise took place, with a corresponding fall after, and finally a gradual approach to normal during convalescence.

Eosinophile corpuscles were present, but only during convalescence, and the polymorpho-nuclear cells were mainly responsible for the increase. There was also an increase in the large mono-nuclear forms, whilst the red corpuscles throughout the whole course of the case were somewhat above the normal.

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CASE NO. 3. M. S. (aet. 13) admitted to hospital on fifth day of illness

Date Nov.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
3	5	103.8°f	104.6°f	3,290,000	80	14	6			4,000
4	6	104	105	3,320,000					4,800	3,400
5	7	104.2	104.2	6,910,000	80	12	8		3,800	3,400
6	8	104	104.8	4,700,000					10,600	12,400
7	9	104.6	104.6	5,680,000	76	17	7		10,100	6,400
8	10	104.2	104.6	5,720,000	77	14	9		14,800	4,200
9	11	103.6	105.2	6,370,000	83	5	12		11,800	9,400
10	12	104.2	105.2	6,040,000	76	10	14		11,200	11,800
11	13	103.2	104	4,600,000	75	14	11		11,600	5,800
12	14	102.6	103	5,330,000	70	16	14		6,800	23,200
13	15	100.6	101.4	7,160,000					7,400	6,600
14	16	98	98	5,530,000	65	20	15		7,000	7,400
15	17	97.6	99	6,800,000					4,800	6,400
16	18	97.6	98	5,250,000	50	37	15		6,600	9,800
18	20	97.2	98.4	7,100,000	54	35	11		8,200	7,000
20	22	97.6	99.2	6,900,000	59	32	9		3,700	4,000
24 Dec.	26	98.2	99	7,000,000	75	17.25	7.5	.25	3,700	3,900
10	42	98	98.4	6,100,000	70	21.5	7.5	1	4,500	4,700

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

3	5	103.8°f	104.6°f	3,200	560	240				4,000
4	6	104	105						4,800	3,400
5	7	104.2	104.2	3,040	456	304			3,800	3,400
6	8	104	104.8						10,600	12,400
7	9	104.6	104.6	7,676	1,717	707			10,100	6,400
8	10	104.2	104.6	11,396	2,072	1,332			14,800	4,200
9	11	103.6	105.2	9,794	590	1,416			11,800	9,400
10	12	104.2	105.2	8,512	1,120	1,568			11,200	11,800
11	13	103.2	104	8,700	1,624	1,276			11,600	5,800
12	14	102.6	103	4,760	1,088	952			6,800	23,200
13	15	100.6	101.4						7,400	6,600
14	16	98	98	4,550	1,400	1,050			7,000	7,400
15	17	97.6	99						4,800	6,400
16	18	97.6	98	3,300	2,442	858			6,600	9,800
18	20	97.2	98.4	4,428	2,870	902			8,200	7,000
20	22	97.6	99.2	2,183	1,184	333			3,700	4,000
24 Dec.	26	98.2	99	2,775	638	278	9		3,700	3,900
10	42	98	98.4	3,150	968	337	45		4,500	4,700

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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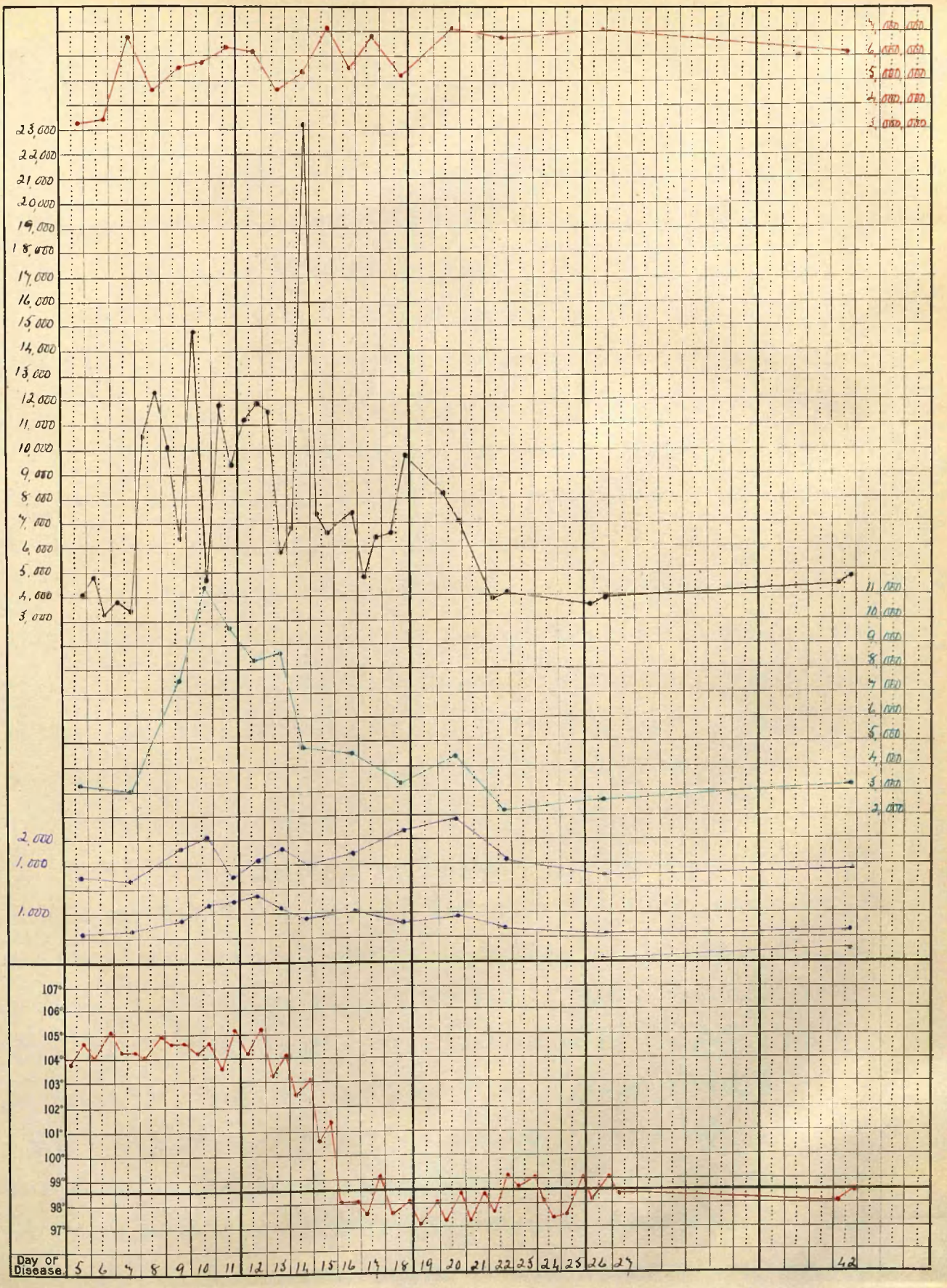
Chart III.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Day of Disease.
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RECOVERIES Contd.

CASE 4. William C., aet. 27, was admitted on 9th November 1902 from the reception house. His temperature was 101° F., pulse rate 112, and respirations 24 per minute.

This is an interesting case because of the fact that patient was admitted to hospital during the latter part of the incubation period of the disease, and as will be seen from the temperature chart, there was a certain degree of pyrexia during the few days immediately preceding the sudden onset, and rise of temperature, usually described as typical of typhus fever.

A typical typhus eruption appeared on 16th November, his (nominally) ninth day of illness, and the disease ran its usual course, the crisis occurring during 26th and 27th November. There was, for about eight days after the crisis, a fluctuating temperature, never above 100° F., but this was due to a bronchitis which manifested itself about a week before the crisis occurred.

The chart is a most interesting one, showing as it does the slight pyrexia during the last few days of the incubation period, and the usual state of matters as regards leucocytosis, viz., a progressive leucocytosis towards the crisis, and a fall thereafter. This fall was more gradual than that noted in the preceding cases, a character probably attributable to the presence of the bronchitis. Again the polymorpho-nuclear cells play the most important part in the increase, and eosinophiles were present from the commencement of the disease. It is of interest to note that, after the crisis, as long as the bronchitis persisted, the large mono-nuclear forms

RECOVERIES Contd.

showed a decided increase, whilst the polymorpho-nuclear cells were diminishing in number. The red cells behaved in a somewhat irregular manner, but were decidedly above the normal throughout.

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CASE NO. 4. W. C. (aet. 27) admitted to hospital during incubation period

Date Nov.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
9		101°f	100.8°f	5,950,000	86	10	4		10,600	13,200
10		100.2	99.4	5,420,000	81.25	7.75	9.75	1.25	8,000	9,800
11		98.4	99.8	4,880,000	70.2	17.2	11.2	1.4	7,400	4,600
12		98.2	98.6	5,100,000					7,200	7,000
14	2	98.6	101.2	7,031,000	82	10.8	6.8	.4	12,400	7,600
15	3	99.4	103.6	6,800,000	85	9.7	5.3		9,800	9,200
16	4	102.8	103	6,500,000	80.8	12.2	7		14,200	12,200
17	5	102.6	104.8	5,050,000	84	6	10		11,400	9,600
18	6	103.4	105.8	6,100,000	88.6	6.8	4.6		17,000	10,200
19	7	102.8	104	6,420,000	91	5.2	3.8		16,400	23,000
20	8	103.6	104	5,083,000	93.6	1.6	4.6	.2	13,200	14,800
21	9	103	104.2	7,900,000	92.5	2	5.5		12,000	15,600
22	10	103.8	103.8	7,260,000	86	5	9		14,200	16,400
23	11	103.6	104.2	7,200,000	87.6	4.4	8		12,800	12,600
24	12	103	102.6	7,500,000	88.8	3.2	8		19,000	18,000
25	13	104.6	103	7,900,000	80	8.5	11.5		13,400	17,000
26	14	103.4	102.8	7,200,000	82.5	6	11.5		14,600	12,600
27	15	100.2	100	7,100,000	82.6	8	9 .2	.2	18,400	22,600
28	16	98.8	99.6	6,900,000	86.6	4.8	8.6		18,200	17,000
29	17	99.2	100	5,750,000	81.7	7.3	10.7	.3	18,200	14,800
30	18	99.4	99.4	5,950,000					16,600	
Dec. 1	19	98.8	99.8	5,500,000	79	10	11		14,800	15,200
2	20	98.8	99.6	6,800,000					13,200	11,600
3	21	99.2	99.2	7,200,000	69	19.5	10.5	1	13,000	13,400
5	23	98.4	98.6	7,350,000	66	24.5	9	.5	12,400	12,400
9	27	98.6	98.6	7,650,000	70	21.75	8	.25	8,000	11,400
15	33	98.4	98.4	6,550,000	67.5	22.5	7.75	2.25	10,200	10,000

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

9		101°f	100.8°f	9,116	1,064	424			10,600	13,200
10		100.2	99.4	6,500	620	780	100		8,000	9,800
11		98.4	99.8	5,195	1,273	829	103		7,400	4,600
12		98.2	98.6						7,200	7,000
14	2	98.6	101.2	10,168	1,329	823	50		12,400	7,600
15	3	99.4	103.6	8,330	951	518			9,800	9,200
16	4	102.8	103	11,474	1,732	994			14,200	12,200
17	5	102.6	104.8	9,576	684	1,140			11,400	9,600
18	6	103.4	105.8	15,062	1,156	782			17,000	10,200
19	7	102.8	104	14,924	853	623			16,400	23,000
20	8	103.6	104	12,355	211	607	27		13,200	14,800
21	9	103	104.2	11,100	240	660			12,000	15,600
22	10	103.8	103.8	12,212	710	1,278			14,200	16,400
23	11	103.6	104.2	11,213	563	1,024			12,800	12,600
24	12	103	102.6	16,872	608	1,520			19,000	18,000
25	13	104.6	103	10,720	1,139	1,541			13,400	17,000
26	14	103.4	102.8	12,045	876	1,679			14,600	12,600
27	15	100.2	100	15,198	1,472	1,693	37		18,400	22,600
28	16	98.8	99.6	15,761	874	1,565			18,200	17,000
29	17	99.2	100	14,869	1,329	1,947	55		18,200	14,800
30	18	99.4	99.4						16,600	
Dec. 1	19	98.8	99.8	11,692	1,480	1,628			14,800	15,200
2	20	98.8	99.6						13,200	11,600
3	21	99.2	99.2	8,970	2,535	1,365	130		13,000	13,400
5	23	98.4	98.6	8,184	3,048	1,116	62		12,400	12,400
9	27	98.6	98.6	5,600	1,740	640	20		8,000	11,400
15	33	98.4	98.4	6,885	2,295	791	229		10,200	10,000

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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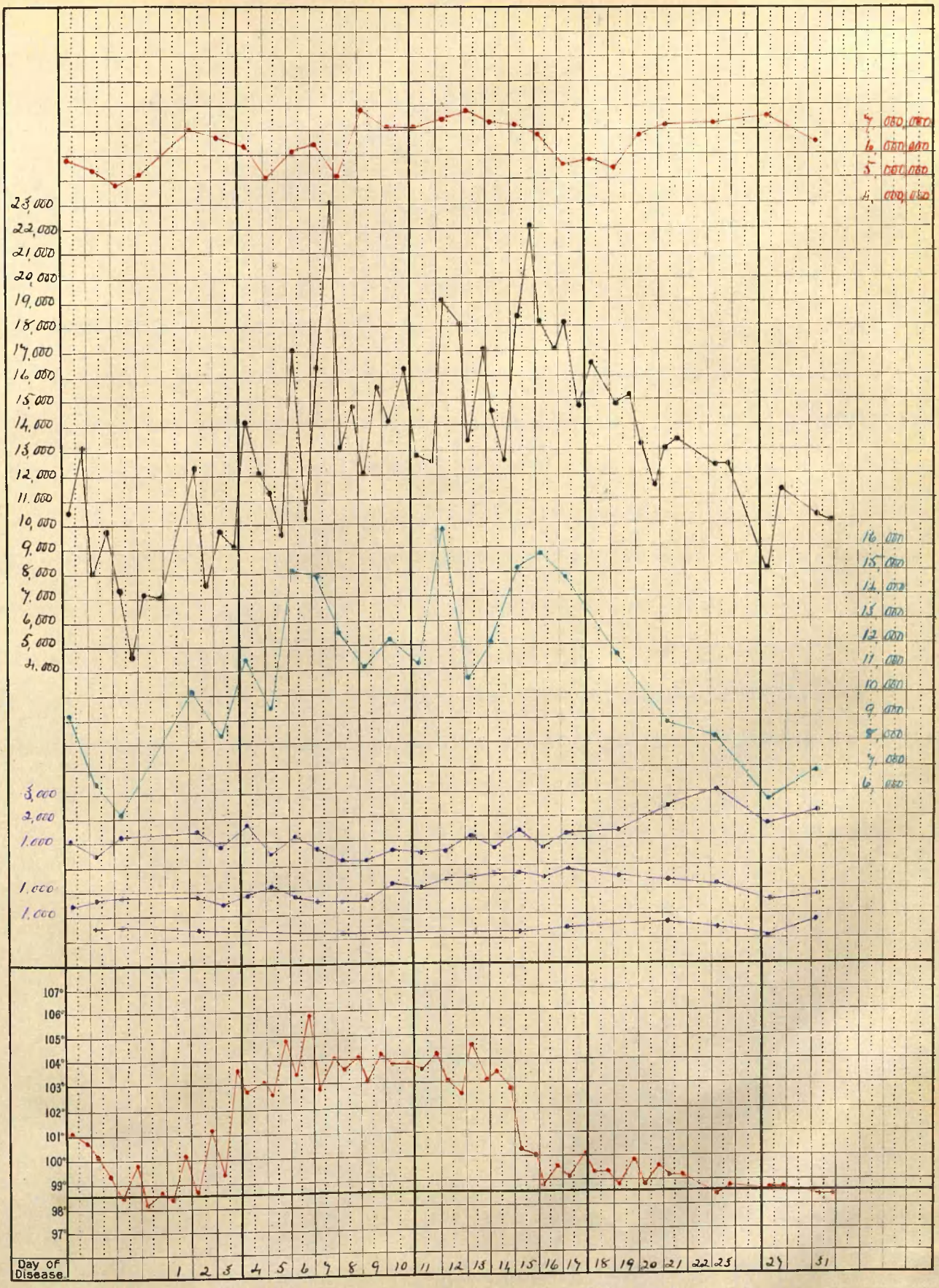
Chart IV.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Day of Disease
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RECOVERIES Contd.

CASE 5. William S., aet. 4, was admitted on 9th November 1902 from the reception house. His temperature was 98.4° F., pulse rate 88, and respirations 24 per minute.

Physical examination of the chest revealed nothing abnormal. A typical typhus eruption appeared on 13th November (fifth day of illness), and the disease ran its usual course, the crisis occurring on 21st November, the thirteenth day of illness.

In this case there was a progressive increase in the leucocytosis towards the crisis, the maximum being reached on the eleventh day of illness: after this the leucocytes began to fall coincidently with the temperature, gradually decreasing in number as convalescence became established. There was also an increase in the large mono-nuclear forms, and eosinophile corpuscles were present from the beginning of the attack.

The red corpuscles were persistently above the normal, and were even more numerous at and immediately after the crisis.

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CASE NO. 5. W. S. (aet. 4) admitted to hospital on first day of illness

Date Nov.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono-Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
10	2	98.6°f	99°f	3,840,000	73	21	5	1	5,200	6,200
11	3	98.6	101.2	5,550,000					6,600	10,000
12	4	100.6	100.2	5,470,000	73	20	7		8,000	5,000
13	5	102.2	103	5,700,000					14,200	5,200
14	6	103.2	103	4,000,000	85	11	4		6,800	7,600
15	7	102.6	104	4,200,000					7,400	19,200
16	8	102.6	102.6	4,600,000	80	12	8		17,200	27,800
17	9	101.4	103.8	4,100,000					27,200	29,600
18	10	100.6	102.8	5,004,000	79	13	8		23,800	22,600
19	11	101.4	101	5,940,000	82	8	10		35,200	42,200
20	12	101.4	101	5,440,000	72	12.15	15	25	27,200	21,000
21	13	99.6	98	6,500,000	73	12	15		17,800	28,000
22	14	97.4	97.6	5,350,000	73	18	8	1	24,600	15,000
23	15	97.6	98.2	4,750,000	64	24	12		15,800	21,600
24	16	98	98.2	5,200,000					28,400	24,800
25	17	97.8	98		58	29	12	1	14,200	16,600
27	19	97.8	98.4	5,750,000	53	34	12	1	15,000	13,400
28	20	97.4	98	6,000,000					13,600	14,800
Dec. 1	23	98	98	6,200,000	66	28.5	5	.5	11,000	15,600
9	31	98	98.4	6,000,000	65	27.5	7	.5	8,200	7,800

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

10	2	98.6°f	99°f	3,796	1,092	260	52	5,200	6,200
11	3	98.6	101.2					6,600	10,000
12	4	100.6	100.2	5,840	1,600	560		8,000	5,000
13	5	102.2	103					14,200	5,200
14	6	103.2	103	5,780	748	272		6,800	7,600
15	7	102.6	104					7,400	19,200
16	8	102.6	102.6	13,760	2,064	1,376		17,200	27,800
17	9	101.4	103.8					27,200	29,600
18	10	100.6	102.8	18,802	3,094	1,904		23,800	22,600
19	11	101.4	101	28,860	2,816	3,520		35,200	42,200
20	12	101.4	101	19,584	3,468	4,080	68	27,200	21,000
21	13	99.6	98	12,994	2,136	2,670		17,800	28,000
22	14	97.4	97.6	17,958	4,428	1,968	246	24,600	15,000
23	15	97.6	98.2	10,112	3,792	1,896		15,800	21,600
24	16	98	98.2					28,400	24,800
25	17	97.8	98	8,236	4,118	1,704	142	14,200	16,600
27	19	97.8	98.4	7,950	5,100	1,800	150	15,000	13,400
28	20	97.4	98					13,600	14,800
Dec. 1	23	98	98	7,260	3,135	550	55	11,000	15,600
9	31	98	98.4	5,330	2,255	574	41	8,200	7,800

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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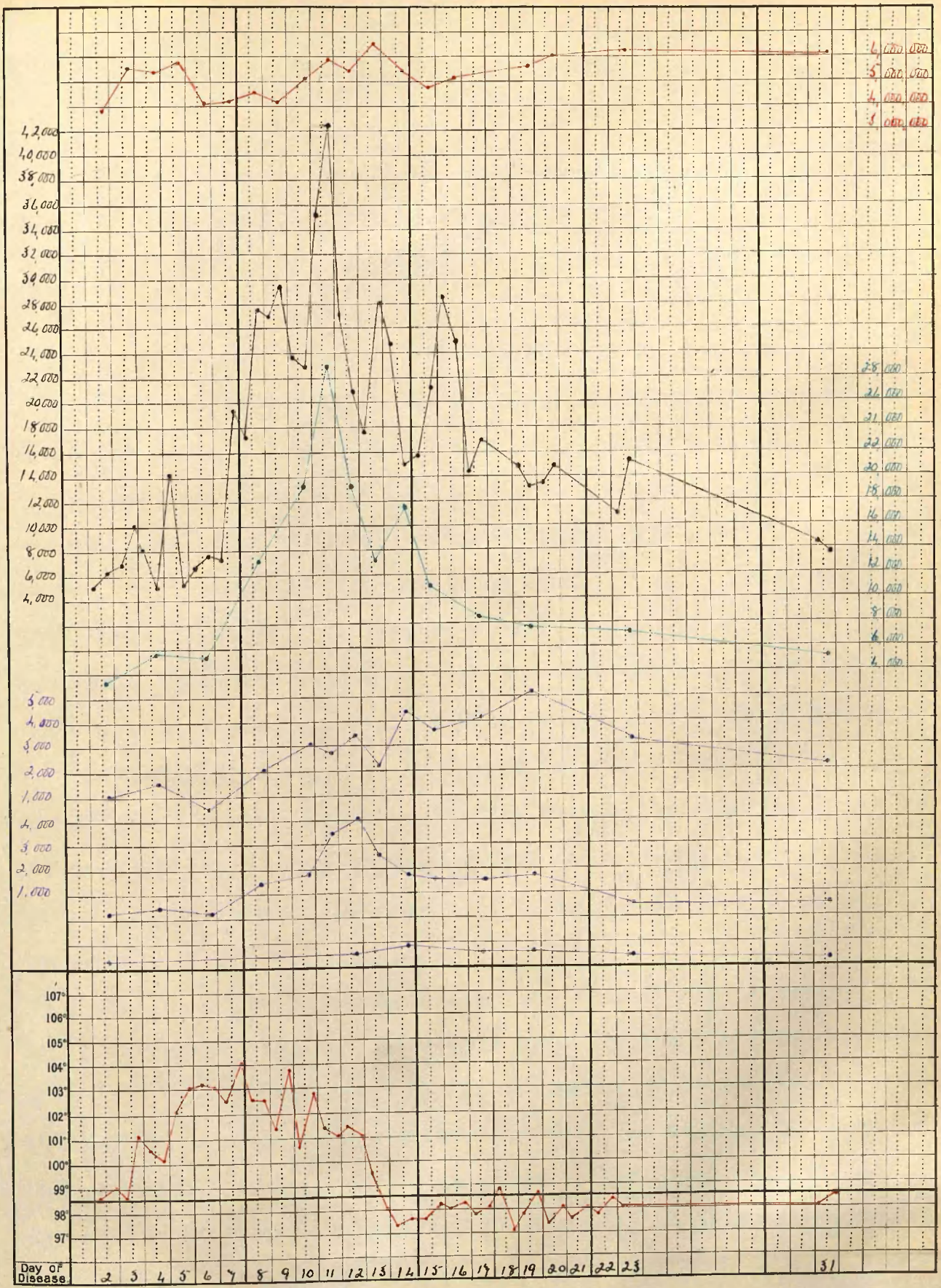
Chart V.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RECOVERIES Contd.

CASE 6. George S., aet. 1 year and 10 months, was admitted to hospital from the reception house on 10th November 1902. His temperature on admission was 101° F., pulse rate 132, and respirations 36 per minute.

The child did not appear seriously ill, and his temperature fell to normal on the following morning: it thereafter fluctuated for a few days, and on 17th November rose suddenly to 103° F. On the morning of the 18th it was normal, but rose to 103° F. in the evening, and after remaining between 101° F. and 104° F. for three or four days, began to fall by lysis until, on 27th November (eleventh day of illness), it reached normal.

This irregular temperature present for the first few days after admission is similar to that seen in Case 4, and probably belongs more properly to the period of incubation rather than to the prodromal stage of the disease. But for this child's association with other cases, it would have been difficult to recognise the true nature of the illness, as there was no rash, and the course of the temperature was most irregular.

The leucocytosis curve is seen to be similarly irregular, but it shows fairly well the characters noted in the preceding cases of this group, viz., the increase in the number of leucocytes towards the end of the attack, the succeeding fall, as well as the fact that the polymorpho-nuclear and large mono-nuclear cells were the main factors in the increase, and lastly, that eosinophile corpuscles were present throughout.

RECOVERIES Contd.

The number of red corpuscles was also fairly high, and increased with the pyrexia.

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CASE NO. 6. G. S. (aet. $1\frac{9}{12}$) admitted to hospital during incubation period

Date Nov.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
11		101°f	102.8°f	5,450,000	71.25	18.75	9.75	.25	14,600	15,000
12		98.4	99	5,640,000					9,200	10,000
14		99	100.8	5,090,000	61	29	9	1	9,400	20,000
15		97	98	5,004,000					16,000	17,600
17	1	99.6	103	5,000,000	17	22.5	7	.5	14,000	12,400
18	2	98.4	103	5,600,000	74	20	6		15,200	16,000
19	3	102	103.4	6,900,000	60	32.5	7.5		18,800	20,000
20	4	101.6	103.6	7,500,000	69.5	22	8.25	.25	20,000	14,200
21	5	101.6	103.8	7,300,000	72.5	19.5	8		15,600	16,000
22	6	102.4	99.8	7,200,000	67	27	6		20,800	10,400
23	7	103	99.6	7,200,000	65	28	7		22,800	17,600
24	8	102	101	6,250,000	68	25	7		17,000	25,800
25	9	99.4	100.2	5,350,000	67.5	27.25	5	.25	13,400	14,600
26	10	100	99.8	6,400,000	62.5	29	8	.5	24,600	23,600
27	11	98.4	98	5,650,000	63	29.5	7	.5	19,400	18,800
28	12	97.6	98	5,300,000	66.5	25	8	.5	23,800	12,800
Dec. 1	13	98.4	97.2	5,250,000					14,400	15,400
3	15	97.8	98.2	5,050,000	70	22	8		17,800	12,400
9	21	98	97.6	6,250,000	67	23	10		14,600	15,200
11	23	97	97.8	5,050,000	65	26.25	8	.75	12,000	12,400
15	27	97.4	98	5,030,000	66.5	24	9	.5	10,800	11,400

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

11		101°f	102,8°f	10,403	2,738	1,423	36	14,600	15,000
12		98.4	99					9,200	10,000
14		99	100.8	5,734	2,726	846	94	9,400	20,000
15		97	98					16,000	17,600
17	1	99.6	103	9,800	3,150	980	70	14,000	12,400
18	2	98.4	103	11,248	3,040	912		15,200	16,000
19	3	102	103.4	11,280	6,110	1,410		18,800	20,000
20	4	101.6	103.6	13,900	4,400	1,650	50	20,000	14,200
21	5	101.6	103.8	11,310	3,042	1,248		15,600	16,000
22	6	102.4	99.8	13,802	5,562	1,236		20,800	10,400
23	7	103	99.6	14,820	6,384	1,596		22,800	17,600
24	8	102	101	11,560	4,250	1,190		17,000	25,800
25	9	99.4	100.2	9,045	3,652	617	33	13,400	14,600
26	10	100	99.8	15,375	7,134	1,968	123	24,600	23,600
27	11	98.4	98	12,222	5,723	1,358	97	19,400	18,800
28	12	97.6	98	15,827	5,950	1,904	119	23,800	12,800
Dec. 1	13	98.4	97.2					14,400	15,400
3	15	97.8	98.2	12,460	3,916	1,424		17,800	12,400
9	21	98	97.6	9,782	3,358	1,460		14,600	15,200
11	23	97	97.8	7,800	3,150	960	90	12,000	12,400
15	27	97.4	98	7,182	2,592	972	54	10,800	11,400

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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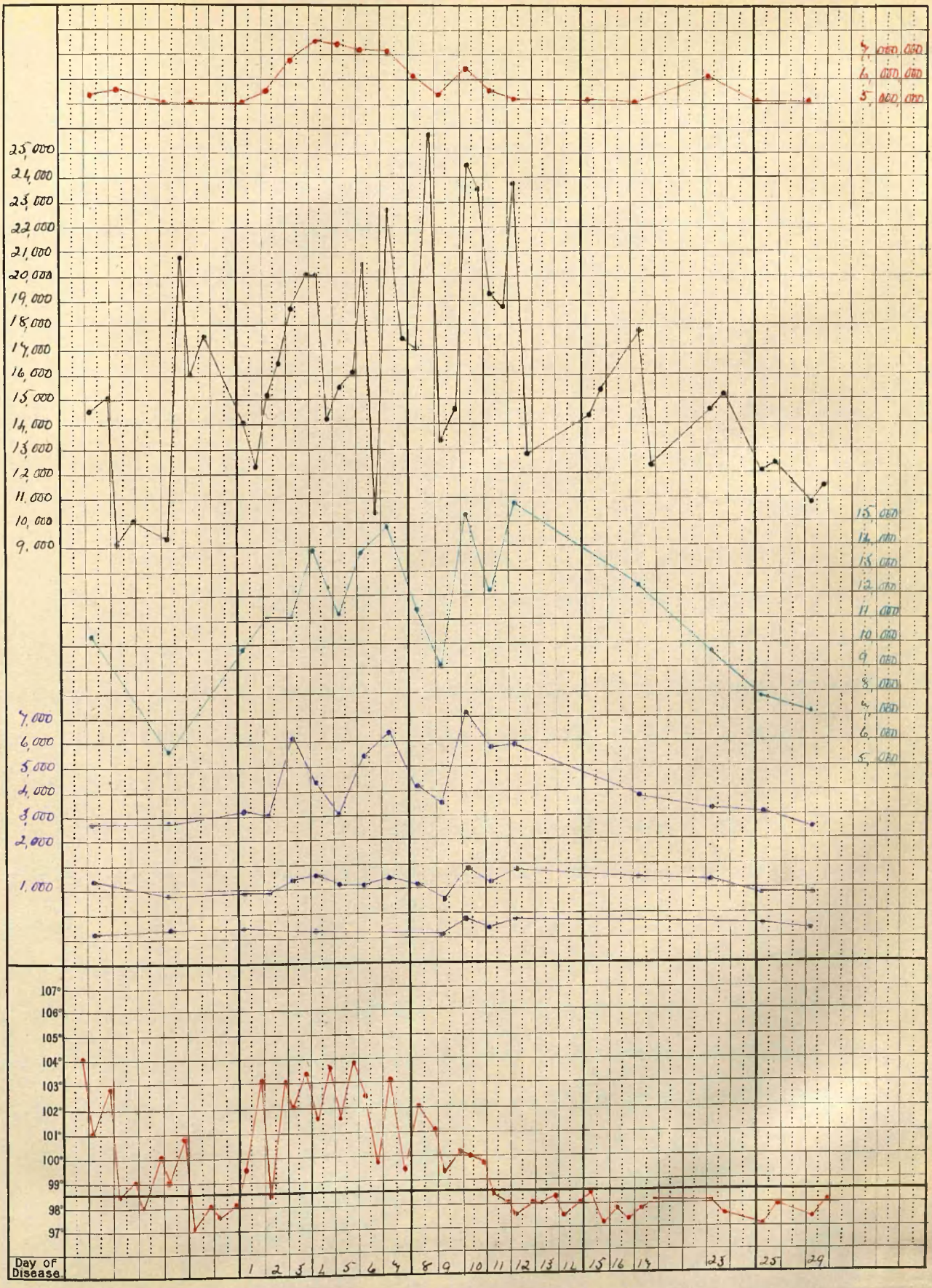
Chart VI.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Day of Disease
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RECOVERIES Contd.

CASE 7. James S., aet. 34, was admitted to hospital on 14th November 1902. His temperature was 99.6° F., pulse rate 104, and respirations 28 per minute. A typical typhus eruption appeared on 17th November (fourth day of illness). The temperature ran high till the seventh day, when it began to subside, and fell to normal on the thirteenth day of illness. The patient was very ill, delirious, and had fallen into the typhoid state. For a few days after the crisis there was marked distension of the abdomen, and he looked as if he might die at any moment.

This patient's chart shows not only the usual increase in the number of leucocytes towards the crisis, with a gradual fall thereafter, but also an increase on the eighth and ninth days, greater even than that seen at the crisis. The explanation of this last fact is not obvious.

The polymorpho-nuclear leucocytes mainly are responsible for the increase, but the large mono-nuclear cells participate in a less degree.

Eosinophiles were found only about ten days after the crisis, but it is important to note that they were present. The red corpuscles during the whole course of the fever were never less than 7,000,000, and at one time they rose as high as 9,000,000 per c.m.

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CASE NO. 7. J. S. (aet. 35) admitted to hospital on first day of illness

Date Nov.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
14	1	99.6°f	102.2°f	7,460,000	71	10	19		6,600	11,400
15	2	102	103	8,050,000					5,000	7,400
16	3	103.8	104	8,700,000	79	10	11		10,600	6,000
17	4	104	103.6	8,500,000					7,600	13,200
18	5	104	105.4	7,700,000	85	6	9		12,000	12,400
19	6	104	104.6	7,075,000					12,800	12,000
20	7	103.4	105.4	7,900,000	84	7	9		11,600	9,200
21	8	102.2	103.2	7,300,000					12,800	26,000
22	9	102	102.2	8,001,000	81	7	12		31,200	22,400
23	10	101.4	102.8	8,100,000					14,400	15,600
24	11	102.6	101	7,600,000	86	6	8		14,200	17,200
25	12	101.4	99.4	9,200,000	86	5	9		19,400	30,200
26	13	99	97.4	7,300,000	87.5	6	6.5		21,300	23,600
27	14	98	98	7,450,000	82.5	11	6.5		16,000	19,600
28	15	98.4	98	7,050,000					21,400	16,600
29	16	98.2	98.2	7,750,000	81	13	6		17,800	16,200
30	17	98	99.2	7,700,000					13,200	13,000
Dec. 1	18	98.4	100	7,000,000	75	18	7		11,000	11,600
2	19	99.2	98.6	7,200,000					6,800	10,400
3	20	98.8	99.4	6,950,000	76	17	7		13,200	10,000
5	22	98.6	97.8	7,250,000	82	11	6.5	.5	12,000	12,200
9	26	99	97.4	6,550.000	80	14	4	2	10,200	7,600
10	27	98	98.6	6,800,000					8,000	8,800

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

14	1	99.6°f	102.2°f	4,686	660	1,254			6,600	11,400
15	2	102	103						5,000	7,400
16	3	103.8	104	8,374	1,060	1,166			10,600	6,000
17	4	104	103.6						7,600	13,200
18	5	104	105.4	10,200	720	1,080			12,000	12,400
19	6	104	104.6						12,800	12,000
20	7	103.4	105.4	9,744	812	1,044			11,600	9,200
21	8	102.2	103.2						12,800	26,000
22	9	102	102.2	24,300	2,100	3,600			31,200	22,400
23	10	101.4	102.8						14,400	15,600
24	11	102.6	101	12,212	852	1,136			14,200	17,200
25	12	101.4	99.4	16,684	970	1,746			19,400	30,200
26	13	99	97.4	18,550	1,272	1,378			21,300	23,600
27	14	98	98	13,200	1,760	1,040			16,000	19,600
28	15	98.4	98						21,400	16,600
29	16	98.2	98.2	14,418	2,314	1,068			17,800	16,200
30	17	98	99.2						13,200	13,000
Dec. 1	18	98.4	100	8,250	1,980	770			11,000	11,600
2	19	99.2	98.6						6,800	10,400
3	20	98.8	99.4	10,032	2,244	924			13,200	10,000
5	22	98.6	97.8	9,840	1,320	780	60		12,000	12,200
9	26	99	97.4	8,160	1,428	408	204		10,200	7,600
10	27	98	98.4						8,000	8,800

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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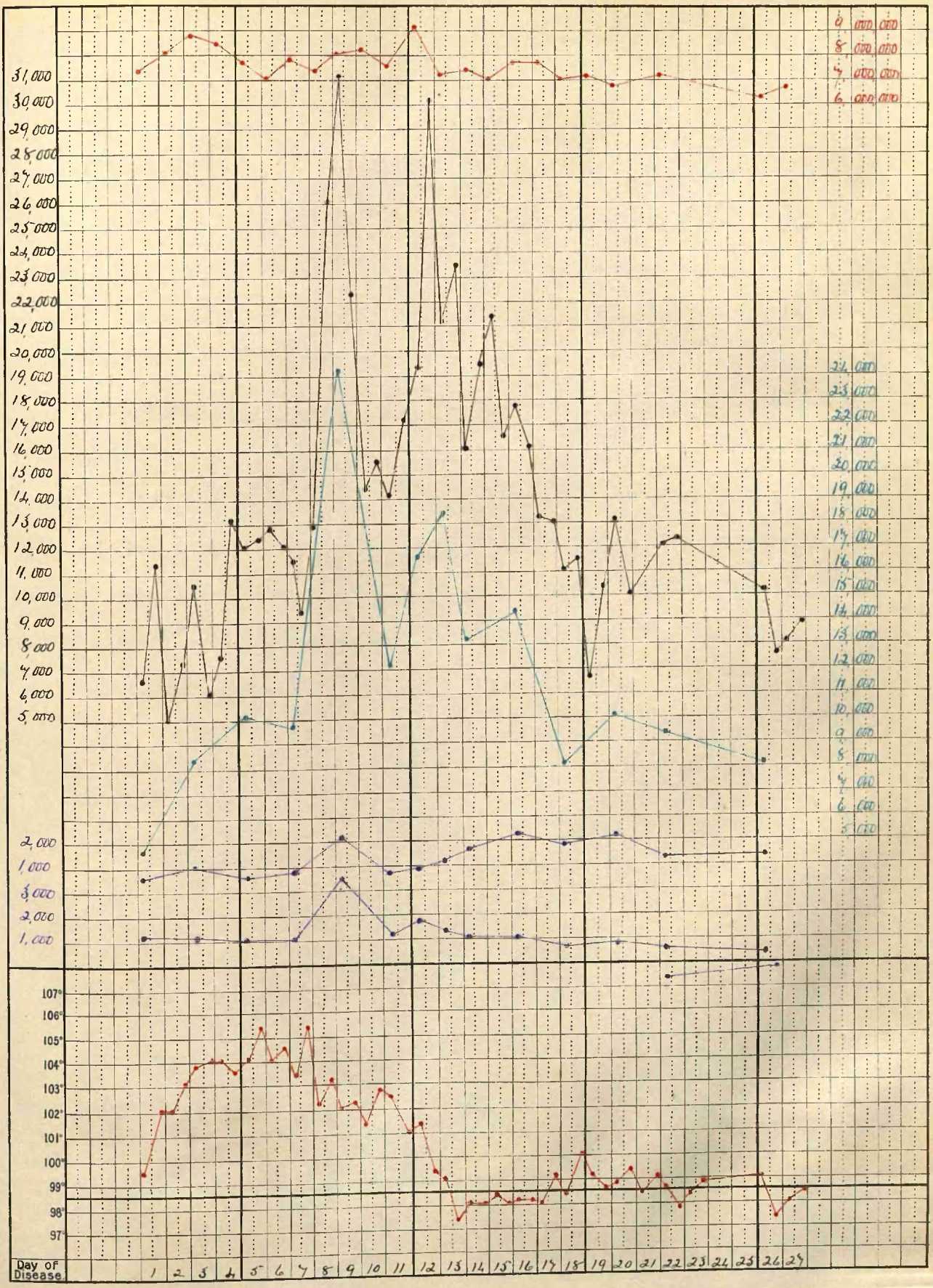
Chart VII.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Day of Disease
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RECOVERIES Contd.

CASE 8. Charles S., aet. 6 months, was admitted on 14th November 1902, his fourth day of illness. His temperature was 98° F., pulse rate 120, and respirations 32 per minute. A typical typhus eruption appeared on the day after admission. The pyrexia, which at times was high, ran a short course, and the crisis occurred on patient's twelfth day of illness. Convalescence was uninterrupted.

The leucocyte chart is somewhat irregular, but if we regard the polymorpho-nuclear corpuscles only, it will be seen that there was present the usual progressive increase towards the crisis, with a fall thereafter. There was also an increase in the number of large mono-nuclear cells and in the eosinophiles, while the red corpuscles were above the normal.

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CASE NO. 8. C. S. (aet. $^{6}/_{12}$) admitted to hospital on fourth day of illness

Date Nov.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono-Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
15	5	99°f	103°f		43	42.8	14.2		18,000	21,000
16	6	103	104	5,890,000	29	51	20		14,400	10,000
17	7	101.8	103.4	4,575,000	59	28.4	12.6		13,800	43,200
18	8	102.6	101.6	4,300,000					33,400	22,400
19	9	102.6	102.2	4,630,000	53	28	19		32,000	29,800
20	10	101.2	102	5,230,000	65	23	12		27,000	24,400
21	11	102.6	101.6	4,100,000	70	20.5	9.5		29,800	32,600
22	12	101.4	99.6	3,600,000	72.5	17.5	10		30,200	26,200
23	13	98	98.4	4,000,000	66	25	9		25,000	23,200
24	14	98	99	4,000,000	56	31.4	11.6	1	27,800	21,800
25	15	98.2	98.8	3,000,000	44	48.4	6	1.6	16,400	30,000
27	17	98.6	99	4,700,000					21,400	22,800
28	18	98.2	98.6	4,500,000	53.5	34.5	11	1	18,800	18,200
Dec. 1	21	98.2	98.8	5,650,000	65	24.5	10	.5	22,600	25,400
9	29	98.4	99	4,070,000	60	30.5	9	.5	12,200	14,600

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

15	5	99°f	103°f	7,740	7,704	2,556			18,000	21,000
16	6	103	104	4,176	7,344	2,880			14,400	10,000
17	7	101.8	103.4	8,142	3,919	1,739			13,800	43,200
18	8	102.6	101.6						33,400	22,400
19	9	102.6	102.2	17,066	9,016	6,118			32,000	29,800
20	10	101.2	102	17,550	6,210	3,240			27,000	24,400
21	11	102.6	101.6	20,860	6,109	2,831			29,800	32,600
22	12	101.4	99.6	21,895	5,285	3,020			30,200	26,200
23	13	98	98.4	16,500	6,250	2,250			25,000	23,200
24	14	98	99	15,560	8,729	3,225	278		27,800	21,800
25	15	98.2	98.8	7,216	7,938	984	262		16,400	30,000
27	17	98.6	99						21,400	22,800
28	18	98.2	98.6	10,593	6,831	2,178	198		18,800	18,200
Dec. 1	21	98.2	98.8	14,690	3,277	2,260	113		22,600	25,400
9	29	98.4	99	7,320	3,721	1,098	61		12,200	14,600

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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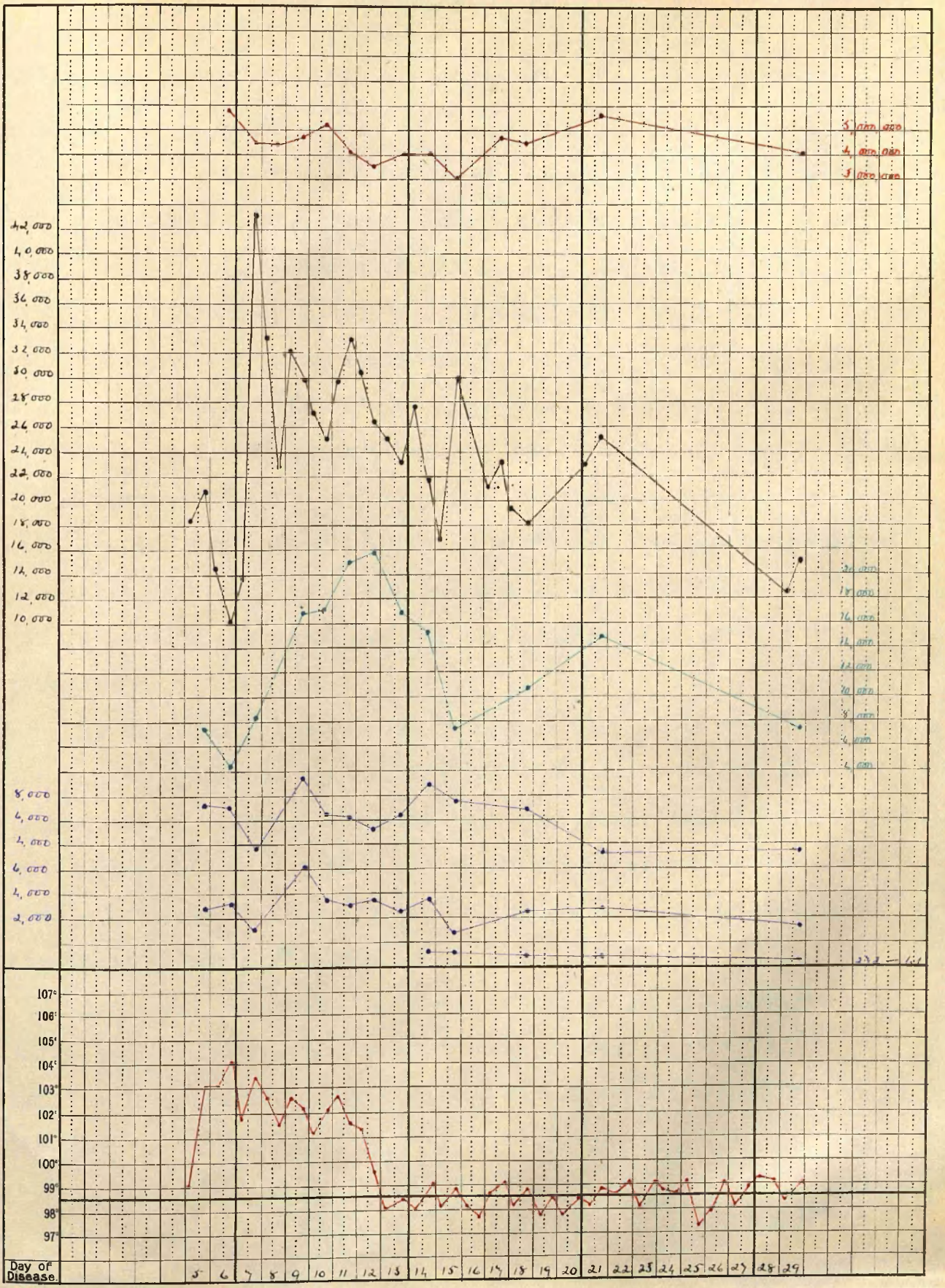
Chart VIII.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RECOVERIES Contd.

CASE 9. Mary McL., aet. 22, was admitted on 20th November 1902, on her fourth day of illness. Her temperature was 103.6° F., pulse rate 104, and respirations 26 per minute. She was sharply ill, and the typical eruption appeared on the day after admission (fifth day of illness). The pyrexia was high throughout the course of the illness, and a fall of four degrees occurred between the fourteenth and fifteenth days. This was evidently the crisis, although it was not until the eighteenth day that the normal temperature was reached.

About a week after the crisis there was some little swelling of patient's left leg, evidently the result of thrombosis of the veins; this gradually subsided, and the subsequent convalescence was uneventful.

In the chart accompanying this case it will be observed that the highest point reached in the leucocyte curve was on the thirteenth day of illness, that the fall took place immediately before and during the crisis, and that there was a secondary rise, with some fluctuation afterwards, which may possibly be attributed to the thrombotic condition in the leg.

The usual features - increase in the polymorpho-nuclear and large mono-nuclear cells, the presence of eosinophile corpuscles, and the great numbers of red cells, will also attract attention in the chart.

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CASE NO. 9. M. McL. (aet. 22) admitted to hospital on fourth day of illness

Date Nov.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono-Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
21	5	104.2°f	104.2°f	6,850,000					9,200	7,000
22	6	103.4	103.4	5,300,000	67	20	13		8,000	10,400
23	7	103.4	104.2	6,000,000					13,800	8,800
24	8	104.6	105.4	6,400,000	80	15	5		10,800	9,800
25	9	104.6	104.6	6,600,000					14,800	9,600
26	10	104	104.6	4,010,000	80	14.8	5.2		9,000	8,800
27	11	103.8	104.8	4,000,000	80	14	6		19,600	19,000
28	12	104.2	104.4	7,200,000	76	17.5	6.5		14,000	12,400
29	13	102.6	103.8	6,850,000	82	13.5	4.5		27,400	10,400
30	14	103.6	105	6,350,000	75	17	8		7,800	8,000
Dec. 1	15	101.2	102	5,150,000	82.75	14	3	.25	7,600	7,200
2	16	100.6	100.8	4,650,000	75	18.5	6.5		4,600	18,000
3	17	100.2	99.8	7,200,000	72	19	8.5	.5	21,400	19,200
4	18	100	98	6,750,000	75	19	6		12,400	10,200
5	19	97.2	98.2	7,250,000	75	19	6		9,800	7,000
6	20	98.2	99.6	5,650,000	73.5	20.75	5.5	.25	8,800	8,600
8	22	98.6	99.4	4,250,000	68	21	10.5	.5	13,000	6,400
9	23	98	98.4	4,660,000	60	32	8		10,000	10,400
13	27	97.8	99	5,950,000	64	30.25	5.5	.25	15,800	9,200
15	29	99	99	5,000,000	65	28.5	6.5		7,400	8,600
17	31	98	98.4	5,450,000	71.25	20	8.5	.25	6,800	7,000

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

21	5	104.2°f	104.2°f						
22	6	103.4	103.4	5,360	1,600			9,200	7,000
23	7	103.4	104.2			1,040		8,000	10,400
24	8	104.6	105.4	8,640	1,620			13,800	8,000
25	9	104.6	104.6			540		10,800	9,800
26	10	104	104.6	7,200	1,332			14,800	9,600
27	11	103.8	104.8	15,680	2,744	468		9,000	8,800
28	12	104.2	104.4	10,640	2,450	1,176		19,600	19,000
29	13	102.6	103.8	22,468	3,699	910		14,000	12,400
30	14	103.6	105	5,850	1,326	1,233		27,400	10,400
Dec. 1	15	101.2	102	6,289	1,064	624		7,800	8,000
2	16	100.6	100.8	3,450	851	228	19	7,600	7,200
3	17	100.2	99.8	15,408	4,066	299		4,600	18,000
4	18	100	98	9,300	2,356	1,819	107	21,400	19,200
5	19	97.2	98.2	7,350	1,862	744		12,400	10,200
6	20	98.2	99.6	6,468	1,826	588		9,800	7,000
8	22	98.6	99.4	8,840	2,730	484	22	8,800	8,600
9	23	98	98.4	6,000	3,200	1,365	65	13,000	6,400
13	27	97.8	99	10,112	4,780	800		10,000	10,400
15	29	99	99	4,810	2,109	869	39	15,800	9,200
17	31	98	98.4	4,845	1,360	481		7,400	8,600
						578	17	6,800	7,000

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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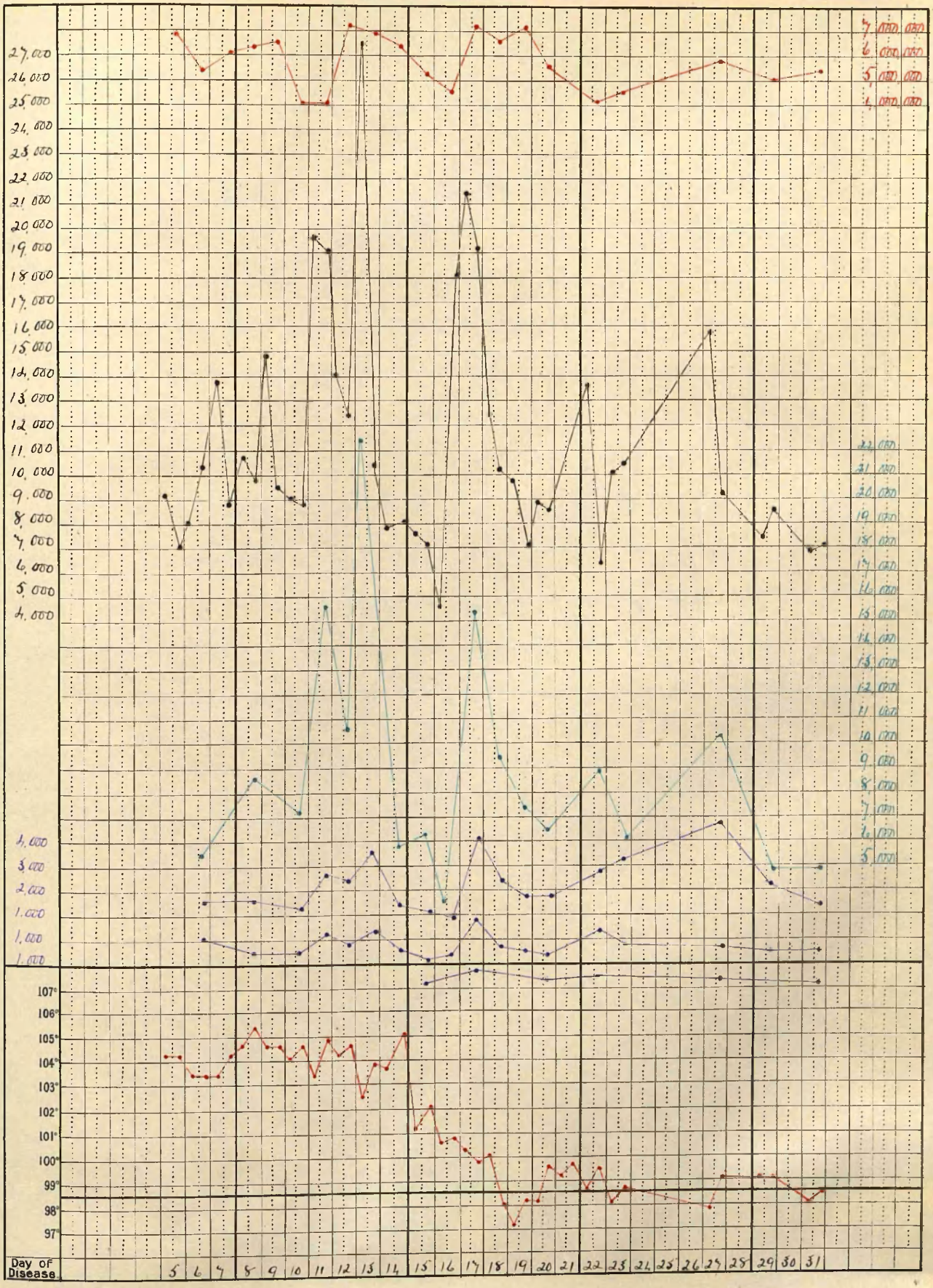
Chart IX.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Day of Disease
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RECOVERIES Contd.

CASE 10. Robert J., aet. 61, was admitted to hospital on 6th December 1902, on his tenth day of illness. His temperature was 102.2° F., pulse rate 120, and respirations 28 per minute. A fixed typhus rash was present all over patient's body. The crisis occurred on the fifteenth and sixteenth days of illness, and convalescence was interrupted only by a slight attack of bronchitis.

The leucocyte chart of this case presents the usual features - a high leucocytosis at or about the crisis, due to an increase in the polymorpho-nuclear elements, with a fall to normal during convalescence. The number of red cells was fairly high in this case as in others of this group, but fell rapidly to normal after the crisis.

Eosinophile corpuscles were found only during convalescence.

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CASE NO. 10. R. J. (aet. 61) admitted to hospital on tenth day of illness

Date Dec.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono-Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
7	11	102.6°f	102.6°f	9,250,000	87.5	6.5	6		17,400	12,400
8	12	102.4	101.6	8,650,000	91.1	5	3.9		17,000	26,400
9	13	101.2	101	8,700,000	88.8	1.6	9.6		13,200	12,200
10	14	99.8	99.2	8,950,000	85.1	3	11.3		19,400	
13	17	97.8	98.4	7,000,000	70.5	12.3	17.2		10,200	8,600
15	19	98.6	98	6,350,000	61.9	21	17.1		7,200	8,000
17	21	98.8	99.4	6,500,000	71.7	16.2	11.8	.3	14,000	14,200
19	23	98.6	100.2	6,100,000	8.33	9.6	6.3	.8	14,000	12,800
22	26	98.2	98.4	6,000,000	62.9	31.7		.7	8,800	8,000

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

7	11	102.6°f	102.6°f	15,225	1,131	1,044		17,400	12,400
8	12	102.4	101.6	15,487	850	663		17,000	26,400
9	13	101.2	101	11,722	211	1,267		13,200	12,200
10	14	99.8	99.2	13,198	462	1,740		19,400	
13	17	97.8	98.4	7,191	1,255	1,754		10,200	8,600
15	19	98.6	98	4,457	1,512	1,231		7,200	8,000
17	21	98.8	99.4	10,038	2,268	1,652	42	14,000	14,200
19	23	98.6	100.2	11,662	1,344	882	112	14,000	12,800
22	26	98.2	98.4	5,535	2,789	414	62	8,800	8,000

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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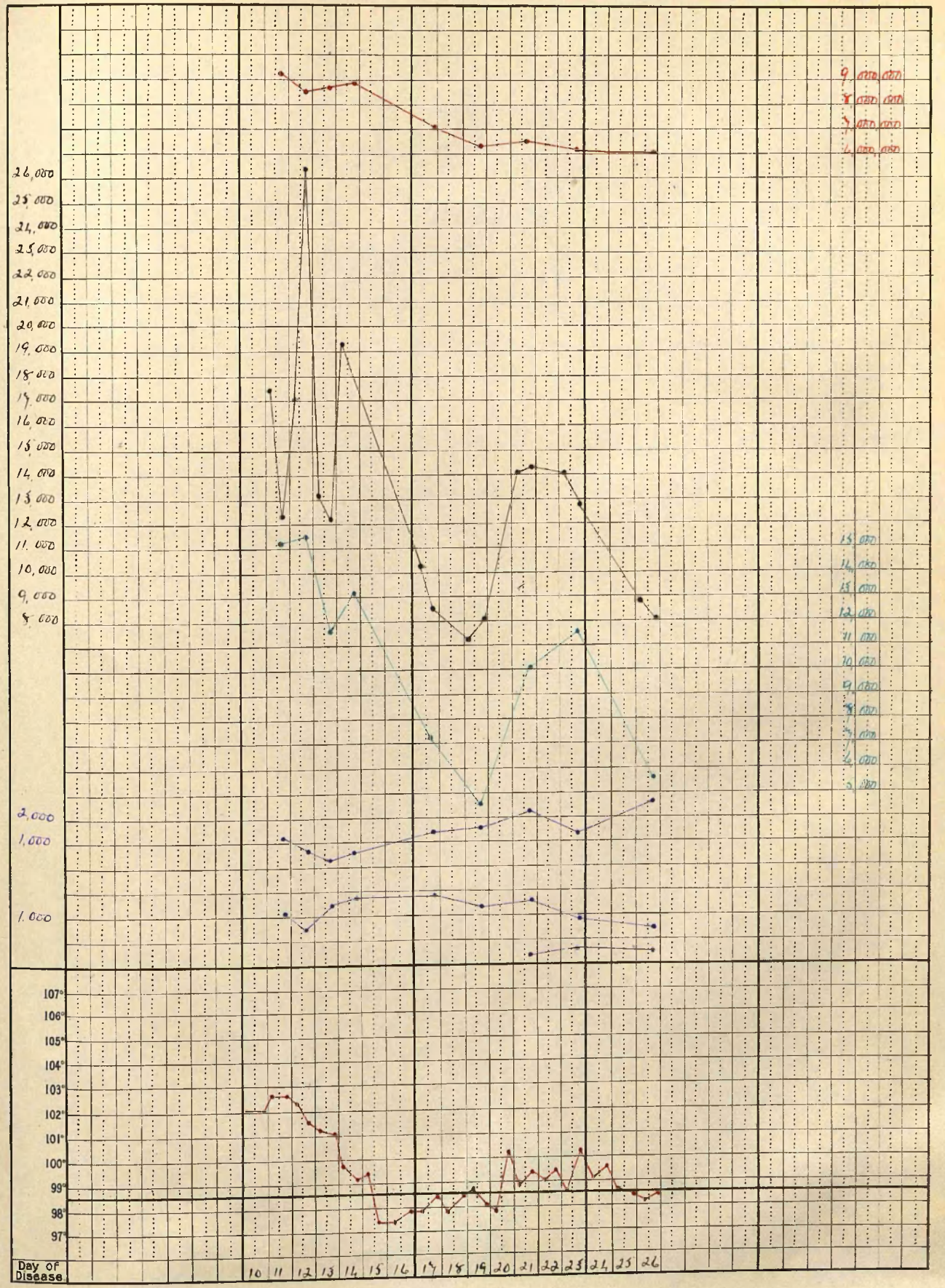
Chart X.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RECOVERIES Contd.

CASE 11. Daniel W., aet. 13, was admitted on 2nd February 1903, that being his ninth day of illness. His temperature was 102.2° F., pulse rate 136, and respirations 32 per minute. The eruption was well developed and mostly fixed. The temperature reached the normal on 8th February (fifteenth day of illness), and convalescence thereafter was uninterrupted.

The chart of this case corresponds in the main with the others, showing a leucocytosis, very high just before the crisis, and a gradual diminution during convalescence.

Eosinophile corpuscles were found in the blood of this case after the crisis, and the increase in leucocytes was due mainly to the polymorpho-nuclear cells. The red cells were not estimated.

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CASE NO. 11. D. W. (aet. 13) admitted to hospital on ninth day of illness

Date Feb.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono-Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
3	10	103.2°f	104°f		83	14	3			19,200
4	11	103.2	103		88	10	2			35,800
5	12	102.6	103.2		87	11	2			14,000
6	13	102	101.8		77	19	4			13,000
7	14	100.2	100.8		83	14	3			12,000
8	15	99.8	98.6							23,800
9	16	99.6	99.8		83	13	3	1		9,400
11	18	98.8	98		85.5	12	2	.5		21,000
13	20	98	98.8		71	26	3			18,000
16	23	97.4	98		68	26	6			9,200
18	25	98	98.4		72	25	3			6,400
The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above										
3	10	103.2°f	104°f		15,936	2,688	576			19,200
4	11	103.2	103		31,504	3,580	716			35,800
5	12	102.6	103.2		12,180	1,540	280			14,000
6	13	102	101.8		10,622	2,622	552			13,000
7	14	100.2	100.8		9,960	1,680	360			12,000
8	15	99.8	98.6							23,800
9	16	99.6	99.8		7,802	1,222	282	94		9,400
11	18	98.8	98		17,955	2,520	420	105		21,000
13	20	98	98.8		12,780	4,680	540			18,000
16	23	97.4	98		6,256	2,392	552			9,200
18	25	98	98.4		4,608	1,600	192			6,400

EXPLANATION OF CHART

Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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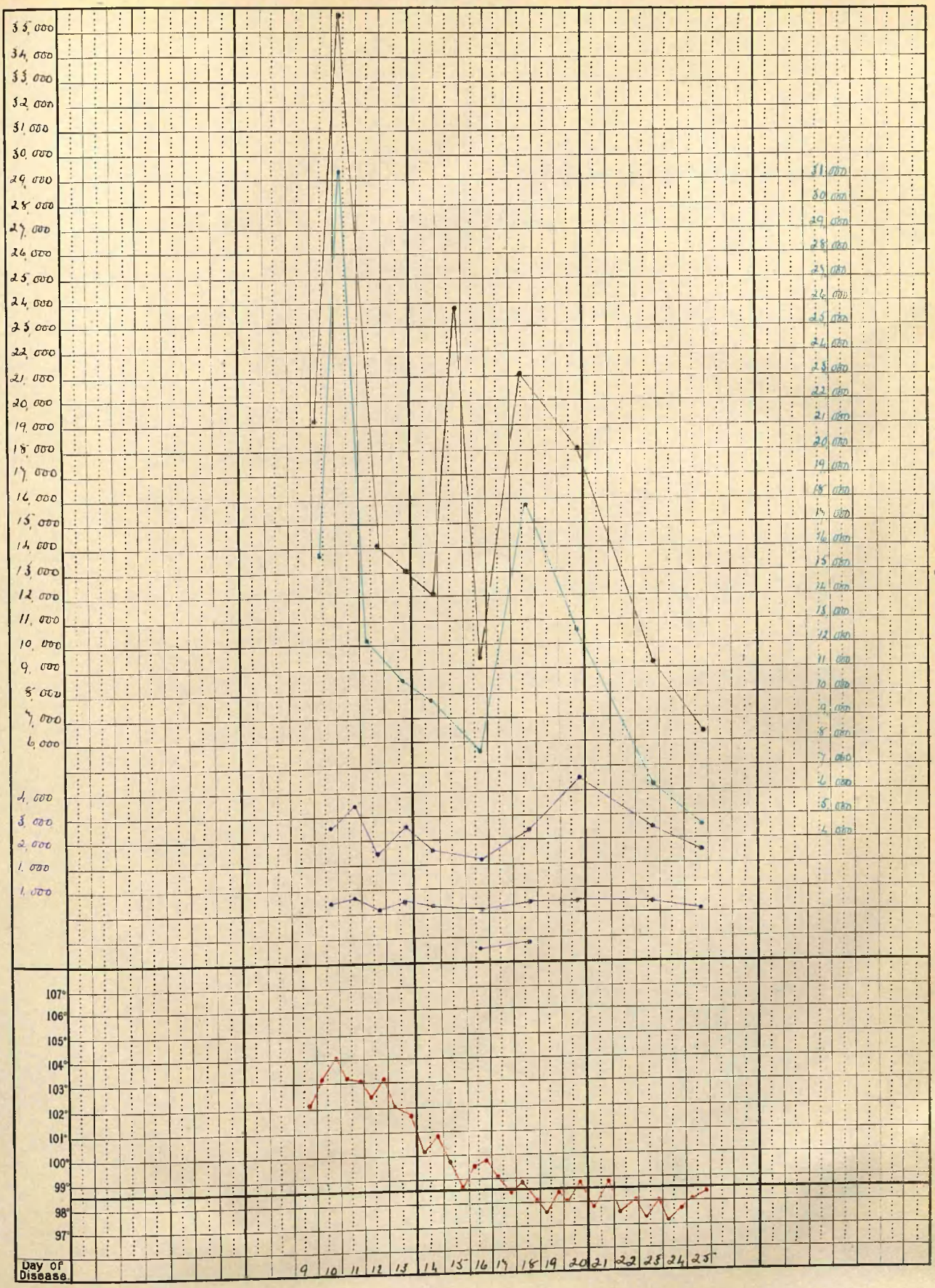
Chart XI.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RECOVERIES Contd.

CASE 12. Mary W., aet. 9, was admitted on 2nd February 1903, that being her ninth day of illness. The eruption was well developed and fixed. Her temperature was 102.2° F., pulse rate 128, and respirations 32 per minute. On the day after admission her temperature rose to 104° F., and then gradually fell until on 8th February (fifteenth day of illness) it was normal, and convalescence thereafter proceeded uninterruptedly.

When estimation of the leucocytes was commenced, their numbers indicated the presence of a leucocytosis in process of decline, as the numbers decreased from day to day coincidently with the fall in temperature.

Eosinophile corpuscles were present during convalescence.

The red cells were not estimated.

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CASE NO. 12. M. W. (aet. 9) admitted to hospital on ninth day of illness

Date Feb.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono-Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes
3	10	104°f	103°f		80	14	6		13,000
4	11	102.6	101.8		78	17	5		9,000
5	12	101.6	102		82	13	5		10,000
6	13	101.8	101.2		81	15	4		12,600
7	14	99.6	99.4		81	14	5		9,400
8	15	99	98.6						9,000
9	16	98.4	99.6		73	22	5		10,000
11	18	98.4	99		74.5	21	4	.5	12,000
13	20	97.6	98.6		62	30			12,600
16	23	97.4	99.8		64.5	30	5	.5	8,600
		The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above							
3	10	104°f	103°f		10,400	1,820	780		13,000
4	11	102.6	101.8		7,020	1,530	450		9,000
5	12	101.6	102		8,200	1,300	500		10,000
6	13	101.8	101.2		10,206	1,890	504		12,600
7	14	99.6	99.4		7,614	1,316	470		9,400
8	15	99	98.6						9,000
9	16	98.4	99.6		7,300	2,200	500		10,000
11	18	98.4	99		8,940	2,520	480	60	12,000
13	20	97.6	98.6		7,812	3,780			12,600
16	23	97.4	99.8		5,547	2,580	430	43	8,600

EXPLANATION OF CHART

Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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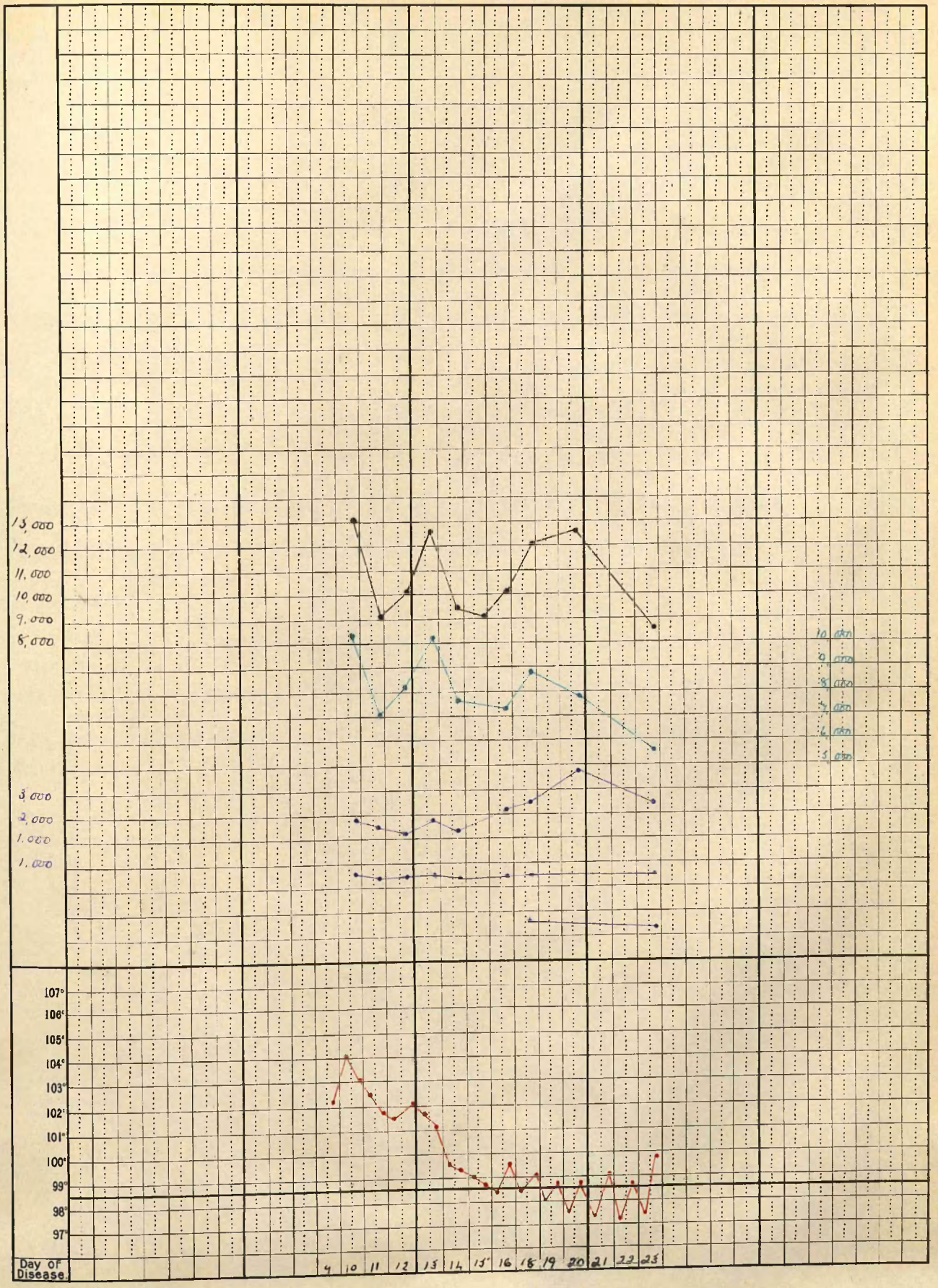
Chart XII.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RECOVERIES Contd.

CASE 13. William W., aet. 11, was admitted to hospital on 3rd February 1903. His temperature was 101.6° F., pulse rate 112, and respirations 32 per minute. The eruption was well developed but not fixed. A fairly high pyrexia was present until the thirteenth day of illness, when the crisis occurred, although the temperature did not reach normal until the sixteenth day of illness.

Unfortunately, estimates were made in this case only when the temperature was falling, but these are sufficient to show that leucocytosis was present, and that the fall usual after the crisis was in progress.

Stained film preparations showed that eosinophiles were present, and that the leucocytosis was mainly due to an increase in the polymorpho-nuclear corpuscles. The red blood cells were not estimated.

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CASE NO. 13. W. W. (aet. 11) admitted to hospital on eighth day of illness

Date Feb.	Day of Illness	Temperatures M	E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono-Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes
9	14	100.6°f	100.2°f		75	20	5		15,000
10	15	98.6	100		73	21	5	1	11,400
11	16	99.8	98		70	19	10	1	9,800
13	18	97.4	98.4		73	20	7		7,800
16	21	97	98.4		70	23	6	1	9,000
18	23	97.4	98		74	22	4		10,400
20	25	97.4	98		74	23	3		9,000

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

9	14	100.6°f	100.2°f		11,250	3,000	750		15,000
10	15	98.6	100		8,322	2,394	570	114	11,400
11	16	99.8	98		6,860	1,862	982	98	9,800
13	18	97.4	98.4		5,694	1,560	546		7,800
16	21	97	98.4		6,300	2,070	540	90	9,000
18	23	97.4	98		7,696	2,288	416		10,400
20	25	97.4	98		6,660	2,070	270		9,000

EXPLANATION OF CHART

Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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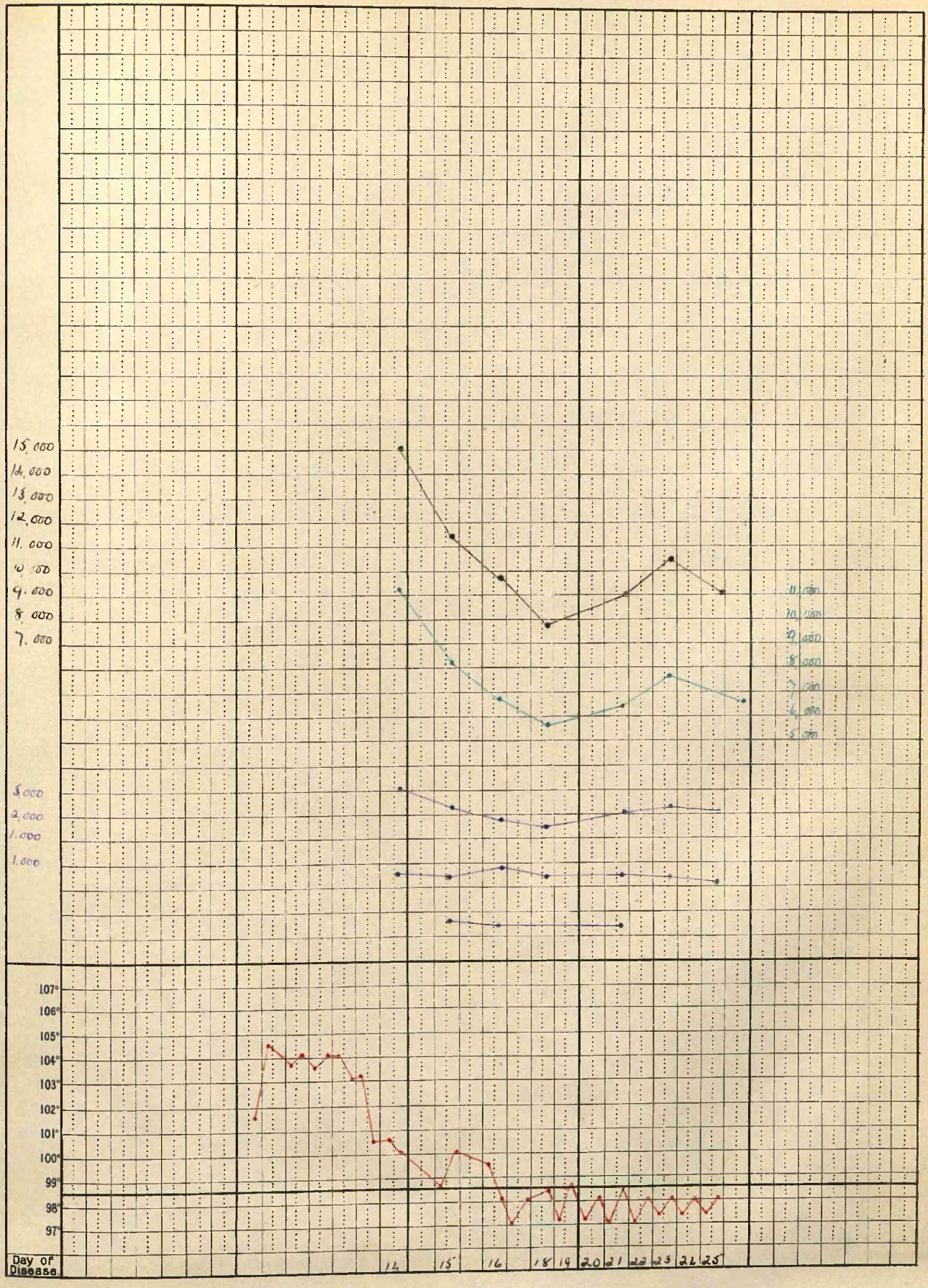
Chart XIII.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RECOVERIES Contd.

CASE 14. Jessie W., aet. 6, was admitted on 3rd February 1903, her seventh day of illness. Her temperature was 101.2° F., pulse rate 120, and respirations 44 per minute. A well developed typhus rash was present, but it was not fixed. The pyrexia was a little irregular, but the crisis occurred during the fourteenth and fifteenth days of illness, and convalescence was quickly established.

The leucocyte chart accompanying this case is not typical. It merely shows the slight secondary rise which sometimes occurs after the crisis, and the gradual approach to normal during convalescence.

The red blood corpuscles were not estimated.

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CASE NO. 14. J. W. (aet. 6) admitted to hospital on seventh day of illness

Date Feb.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono-Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes
9	13	101°f	102.2°f		71	21	8		9,200
10	14	99.4	98.4		69	24	6	1	12,000
11	15	98	98		61	29	9	1	12,600
13	17	97	98.4		53	41	5	1	10,000
16	20	97.6	98.6		50	45	4.5	.5	8,600
18	22	97.6	98.4		52.5	42	5	.5	8,800

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

9	13	101°f	102.2°f		6,532	1,932	736		9,200
10	14	99.4	98.4		8,280	2,880	720	120	12,000
11	15	98	98		7,686	3,654	1,134	126	12,600
13	17	97	98.4		5,300	4,100	500	100	10,000
16	20	97.6	98.6		4,300	3,870	387	43	8,600
18	22	97.6	98.4		4,620	3,696	440	44	8,800

EXPLANATION OF CHART

Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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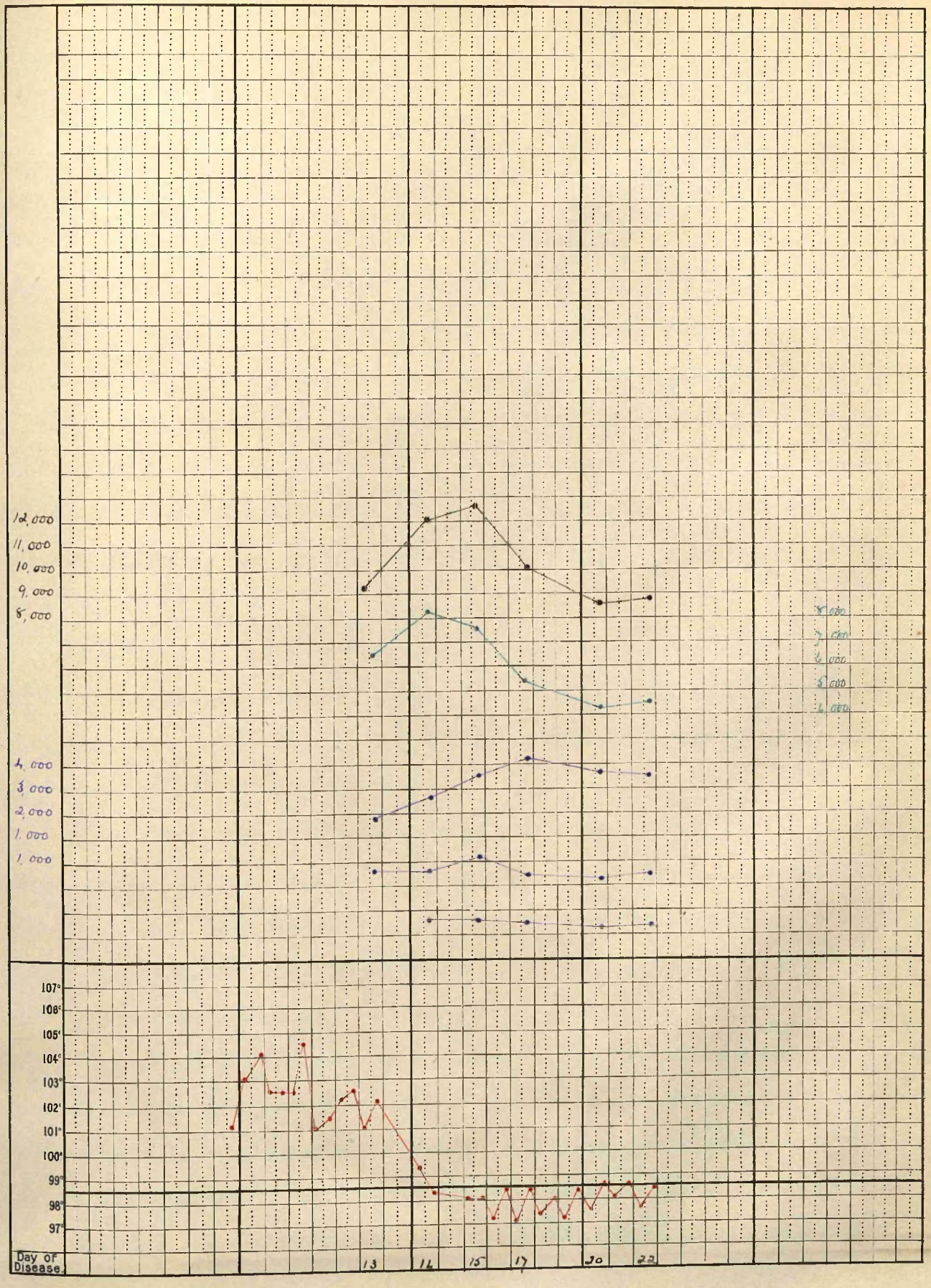
Chart XIV.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Day of Disease.
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RECOVERIES Contd.

CASE 15. William C., aet. 4, was admitted on 7th October 1903, his fifth day of illness. His temperature was 103° F., pulse rate 132, and respirations 32 per minute. Subcuticular mottling was present all over the body, and a typical though not abundant typhus eruption appeared on the day after admission. The temperature ran practically between 102° F. and 103° F., until the eleventh day when there was a fall of almost two degrees towards morning. The same night however it again rose to 102° F., and next morning (twelfth day of illness) the crisis occurred, the temperature falling from 102° F. to 99.2° F.

Owing to an attack of bronchitis which manifested itself about the ninth day of illness, the temperature did not remain normal, but fluctuated between 98° F. and 103° F., until the nineteenth day of illness when it became settled.

The leucocyte count shows a steady rise in the number of white cells, the highest record being on the day of the crisis, whilst on the following day there was a marked fall. Thereafter the leucocytosis fluctuated until the bronchitis became quiescent, after which the numbers recorded were normal.

The chart also shows in an interesting manner the effect of the bronchitis on the lymphocytes. These cells are known to be increased in numbers in bronchial affections, and here it is seen that they were markedly increased during the period in which the bronchitis was active. The presence of the large mono-nuclear and eosinophile corpuscles will also be noted.

CASE NO. 15. W. C. (aet. 4) admitted to hospital on 7th October, 1903, on his fifth day of illness

Date Oct.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono-Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
8	6	102.2°f	102.8°f	4,310,000	56	32	12		10,000	
9	7	103	103.2	5,000,000	67	26	7		9,400	9,000
10	8	102.4	103.4	4,460,000	66	28	6		12,000	11,200
11	9	101.4	102.4	4,580,000	65	31	4		14,000	14,000
12	10	102	102	4,550,000	74	23	3		14,000	13,000
13	11	100.4	102	4,070,000	65	31.5	3.5		11,400	15,000
14	12	99.2	103	5,280,000	69	28	3		16,400	18,000
15	13	100.4	102.6	4,840,000	65	32	3		11,000	13,000
16	14	101.4	101.6	4,950,000	55.5	38	6	.5	14,000	8,400
18	16	99	101.8	4,750,000	60	34	5	1	13,000	8,800
20	18	98	100.2	5,000,000	46	49.5	4	.5	12,800	9,200
22	20	98	97.2	4,750,000	44	50	6		11,600	10,000
24	22	98	98	4,900,000	45	51	4		10,200	9,000
27	26	98	98.4	4,500,000	58.5	35	6	.5	8,800	8,500

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

8	6	102.2°f	102.8°f	4,310	5,600	3,200	1,200		10,000	
9	7	103	103.2		6,298	2,444	658		9,400	9,000
10	8	102.4	103.4		7,920	3,360	720		12,000	11,200
11	9	101.4	102.4		9,100	4,340	560		14,000	14,000
12	10	102	102		10,360	3,220	420		14,000	13,000
13	11	100.4	102		7,410	3,591	399		11,400	15,000
14	12	99.2	103		11,040	4,480	480		16,400	18,000
15	13	100.4	102.6		7,150	3,520	330		11,000	13,000
16	14	101.4	101.6		7,770	5,320	840	70	14,000	8,400
18	16	99	101.8		7,800	4,420	650	130	13,000	8,800
20	18	98	100.2		5,888	6,336	512	64	12,800	9,200
22	20	98	97.2		5,104	5,800	696		11,600	10,000
24	22	98	98		4,590	5,202	408		10,200	9,000
27	26	98	98.4		5,148	3,080	528		8,800	8,500

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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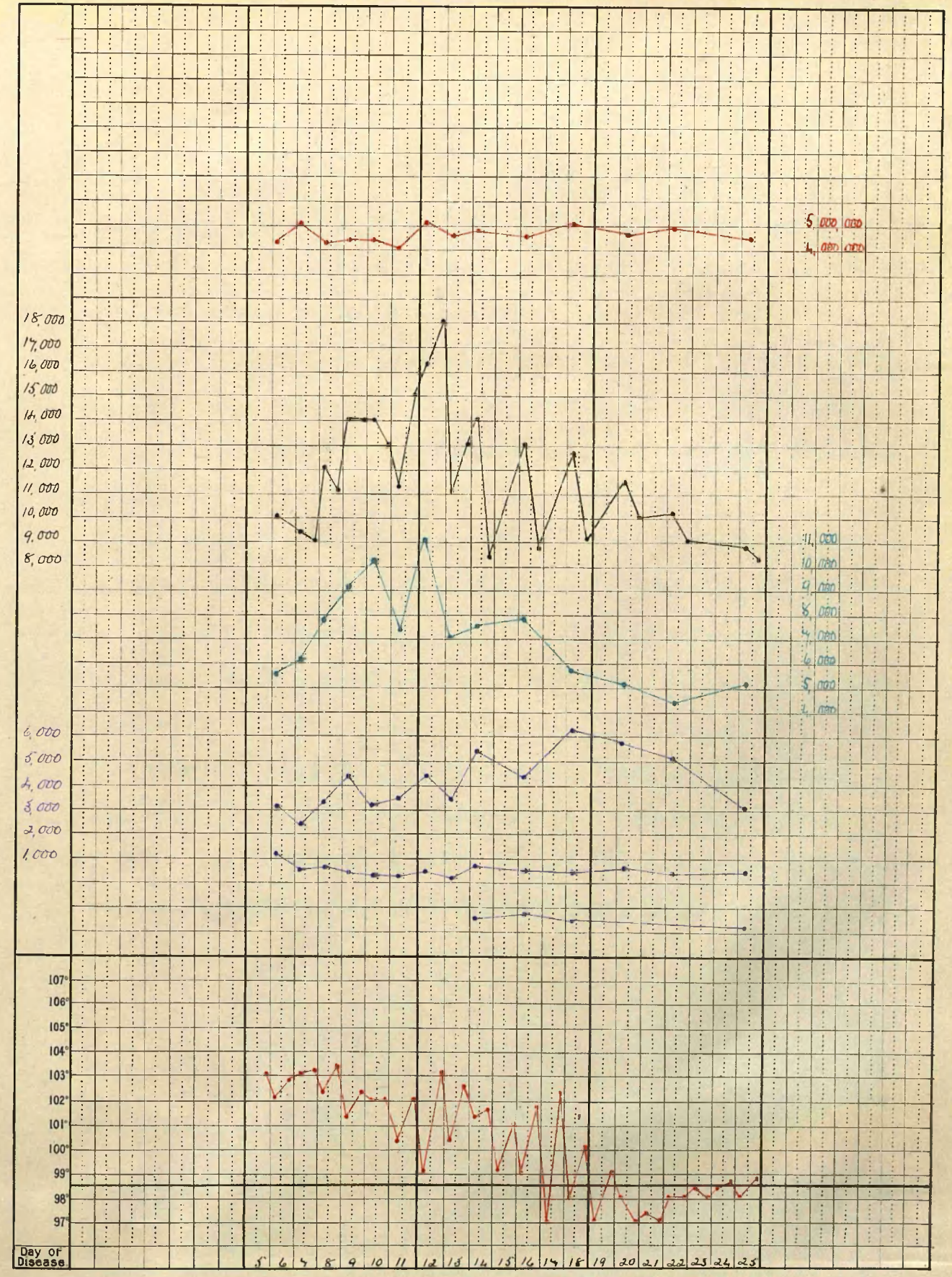
Chart XV.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RECOVERIES Contd.

CASE 16. Jeanie K., aet. 28, was admitted on 12th October 1903, that being her ninth day of illness. Her temperature was 103.8° F., pulse rate 120, and respirations 34 per minute. There was a typical and abundant typhus eruption all over the body and limbs. The temperature did not pursue a typical course, but fluctuated greatly, falling by a prolonged lysis till it became normal on the twenty-first day of illness. During this thme the patient was very sharply ill, and at times delirious.

The accompanying chart shows two distinct rises and falls in the number of leucocytes. The first fall is somewhat difficult to explain, but the second is the usual occurrence after the crisis. In this case the decline is gradual, and practically accompanies the temperature.

It is to be noted that the polymorpho-nuclear cells play the most important part, and that eosinophile corpuscles were found only during the stage of convalescence, whilst the red cells were higher than normal throughout the whole of the acute phase.

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CASE NO. 16. J. K. (aet. 28) admitted to hospital 12th October, 1903, on her ninth day of illness

Date Oct.	Day of Illness	Temperatures M	Temperatures E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono-Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	Total No. of Leucocytes E
12	9	103.8°f	104°f	6,600,000					15,200	24,000
13	10	102.8	104.4	8,000,000	80	12.5	7.5		20,200	22,000
14	11	101.4	104	8,350,000	88	7	5		11,400	12,800
15	12	101	102.4	7,500,000	82	8	10		19,600	20,800
16	13	101.8	103	8,000,000	70	15	15		22,000	
18	15	100.4	101.6	8,150,000	76	9	15		24,000	17,200
19	16	100.2	101	8,880,000	73	12	15		16,400	17,000
20	17	100.2	99.2	7,700,000	75	11	14		16,400	15,000
21	18	99.2	100.6	6,770,000	79	16	5		14,000	14,500
22	19	99.2	100.4	6,800,000	82	11	7		15,600	11,200
24	21	98.4	98.6	6,000,000	72.5	19.5	8		8,000	4,000
26	23	97.4	99	5,850,000	70	22.5	7	.5	8,500	8,000
28	25	98	98	5,500,000	62.5	25	12	.5	8,200	8,000

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

12	9	103.8°f	104°f						15,200	24,000
13	10	102.8	104.4	16,160	2,525	1,515			20,000	22,000
14	11	101.4	104	10,032	798	570			11,400	12,800
15	12	101	102.4	16,072	1,568	1,960			19,600	20,800
16	13	101.8	103	15,400	3,300	3,300			22,000	
18	15	100.4	101.6	18,240	2,160	3,600			24,000	17,200
19	16	100.2	101	11,972	1,968	2,460			16,400	17,000
20	17	100.2	99.2	12,300	1,804	2,296			16,400	15,000
21	18	99.2	100.6	11,060	2,240	700			14,000	14,500
22	19	99.2	100.4	12,792	1,716	1,092			15,600	11,200
24	21	98.4	98.6	5,800	1,560	640			8,000	4,000
26	23	97.4	99	5,950	1,912	595	43		8,500	8,000
28	25	98	98	5,125	2,050	984	45		8,200	8,000

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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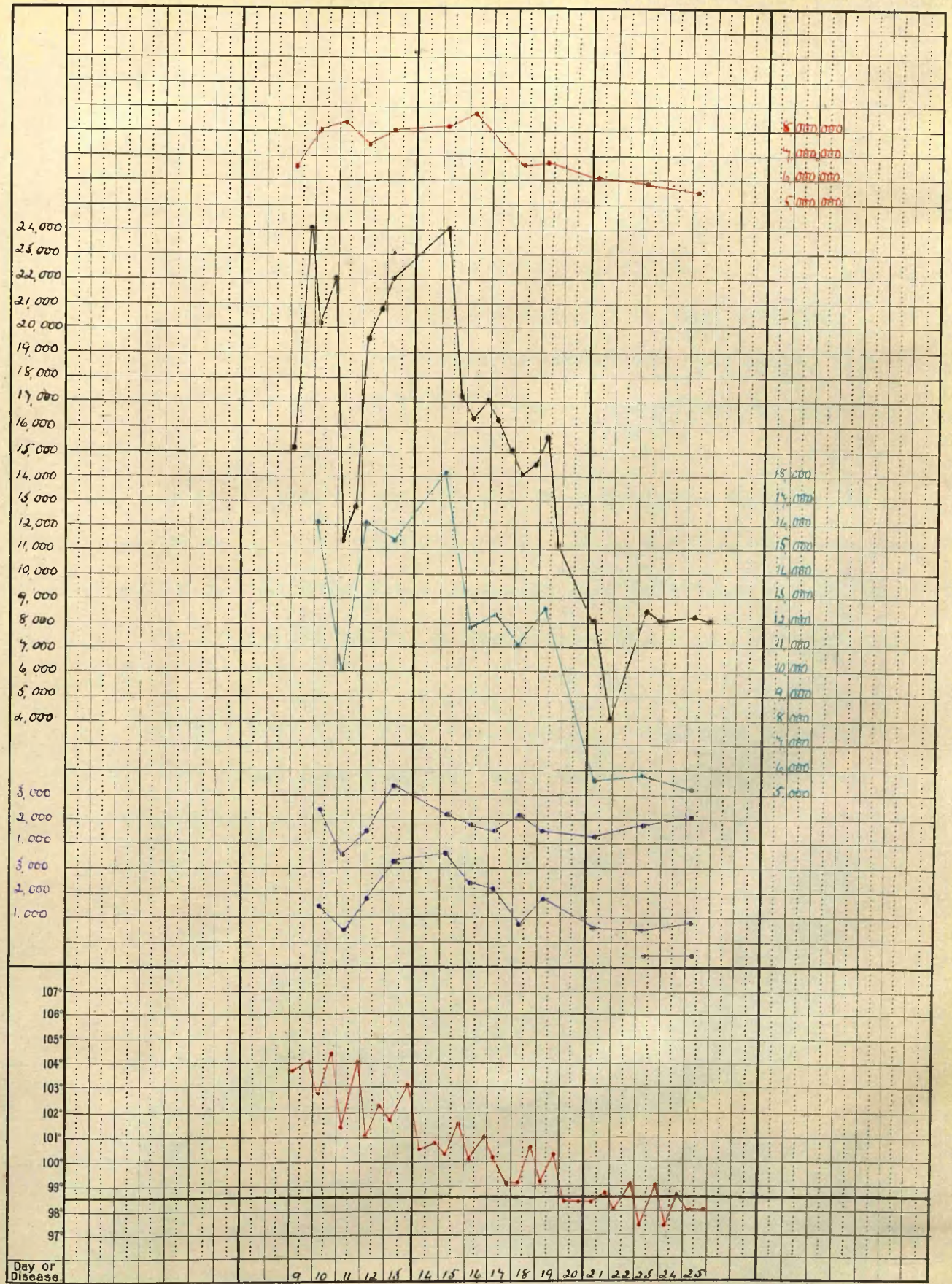
Chart XVI.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Day of Disease
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RECOVERIES Contd.

CASE 17. Lettie G., aet. 21, was admitted to hospital on 12th October 1903, her twelfth day of illness. Her temperature was 103.6° F., pulse rate 124, and respirations 32 per minute. She was sharply ill, and there was an abundant fixed typhus eruption all over the trunk and limbs. The crisis occurred on the fourteenth and fifteenth days of illness, and convalescence thereafter was quick and uninterrupted.

The leucocyte chart demonstrates in a striking fashion the great rise which usually occurs at the crisis and the corresponding fall afterwards. In this case, however, the fall took place immediately before the crisis began, a phenomenon which has already been alluded to.

It will be noted also that eosinophile corpuscles were found in nearly all the films examined, and that the red corpuscles were at no time diminished in numbers.

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CASE NO. 17. L. G. (aet. 21) admitted to hospital 12th October, 1903, on her twelfth day of illness

Date Oct.	Day of Illness	Temperatures M	E	Red Cells	Polymorpho Nuclear Cells per cent.	Lymphocytes per cent.	Large Mono-Nuclear Cells per cent.	Eosinophile Cells per cent.	Total No. of Leucocytes M	E
13	13	102.2°f	103.4°f	5,340,000	78	19	3		15,600	27,000
14	14	101.8	103.6	7,200,000	85	10	4	1	11,400	12,000
15	15	99.4	100.8	5,990,000	76	18.5	5.5		16,000	12,600
16	16	98.4	98	5,250,000	70	25	4	1	12,000	10,800
18	18	97.6	98	5,000,000	60	34.8	4	1.2	8,400	8,600
20	20	98	98.4	5,500,000	61	35	4		9,200	10,000
23	23	97	99	5,030,000					12,000	10,000
25	25	98	98.2	4,900,000	74	21	4	1	8,500	7,000

The following are the Absolute Numbers of the different varieties of Leucocytes calculated from the above

13	13	102.2°f	103.4°f		12,168	2,964	468		15,600	27,000
14	14	101.8	103.6		9,690	1,140	456	114	11,400	12,000
15	15	99.4	100.8		12,160	2,960	880		16,000	12,600
16	16	98.4	98		8,400	3,000	480	120	12,000	10,800
18	18	97.6	98		5,040	2,923	336	101	8,400	8,600
20	20	98	98.4		7,320	4,200	480		9,200	10,000
23	23	97	99						12,000	10,000
25	25	98	98.2		6,290	1,785	340	85	8,500	7,000

EXPLANATION OF CHART

Red Corpuscles	in Red
Total Number of Leucocytes	in Black
Polymorpho-nuclear Leucocytes	in Green
Large Mono-nuclear Leucocytes	in Violet
Lymphocytes	in Violet
Eosinophiles	in Violet
Temperature Chart	in Red

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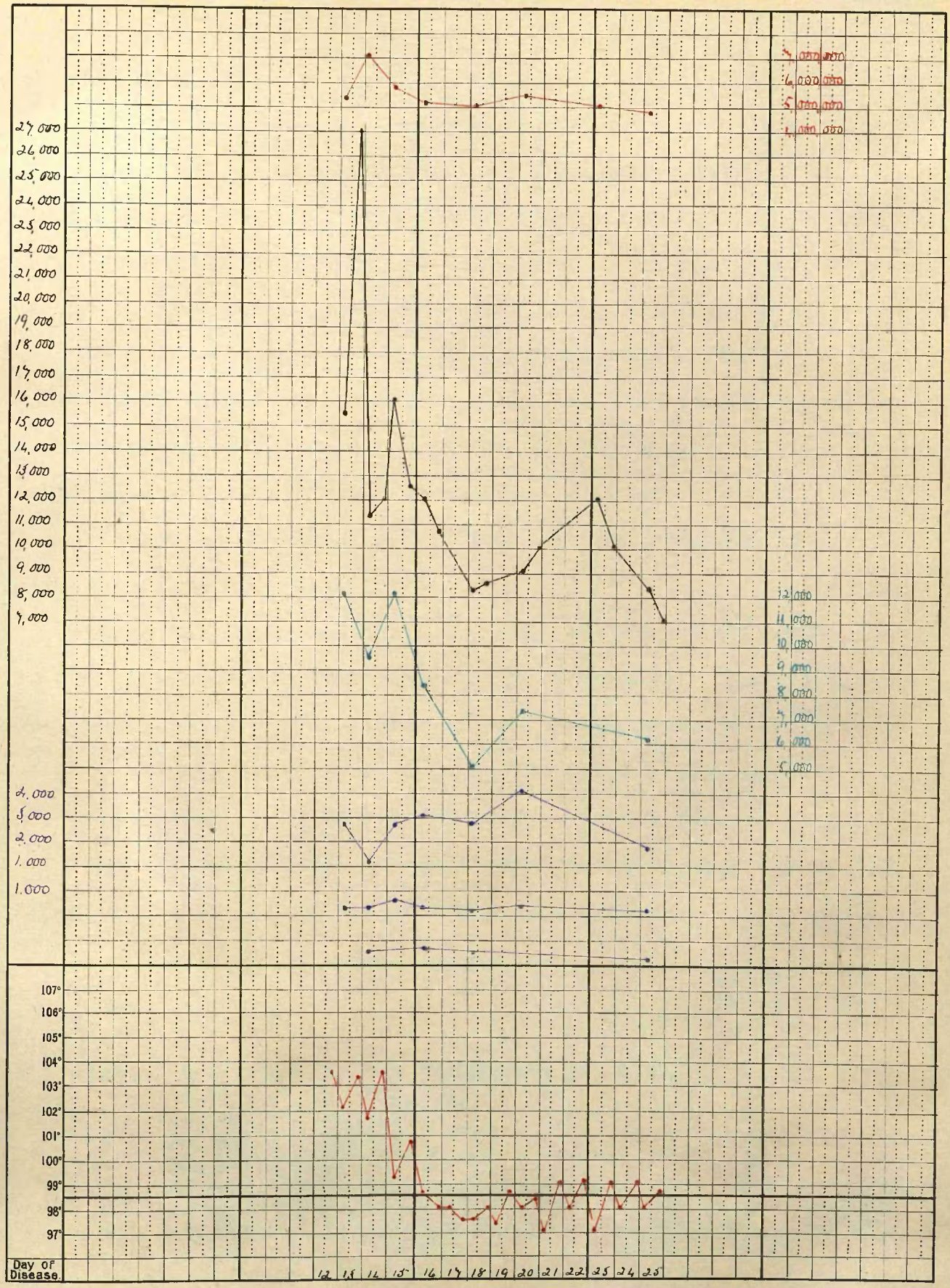
Chart XVII.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Day of Disease
12 13 14 15 16 17 18 19 20 21 22 23 24 25

The foregoing charts have been prepared to show graphically the results of the estimates of the different corpuscles in the fresh blood, along with the absolute numbers in which each variety occurs.

Each chart is accompanied by an explanatory note.

If we accept 7,000 to 8,000 leucocytes per c.m. of peripheral blood as a normal standard, it will be observed that the black line on the charts (total leucocytes) constantly indicates a number in excess of this; in other words a leucocytosis was always present. In addition it should be noted that the black line (total leucocytes), and the green (polymorpho-nuclear cells) run almost parallel to each other throughout the series of charts; in other words, the leucocytosis is due to an increase both absolute and relative of the polymorpho-nuclear neutrophiles.

It has already been indicated that the degree of leucocytosis in the cases recorded was generally considerable. The average maximum leucocytosis of the series of twenty-six cases is found to be 24,000, but the maximum estimate in the fresh blood, made in the different cases, will be seen to vary between 8,000 and 54,000.

The following table has been constructed to show the maximum leucocytosis of the series of twenty-six cases:-

						No. of Cases	No. of Deaths
Between	8,000	and	15,000	leucocytes	per c.m.	7	4
"	15,000	"	20,000	"		3	0
"	20,000	"	25,000	"		3	0
"	25,000	"	30,000	"		5	1
"	30,000	"	35,000	"		3	2
"	35,000	"	40,000	"		1	0
"	40,000	"	45,000	"		3	1
"	45,000	"	55,000	"		1	1
Above	55,000					0	0

An analysis of the foregoing clinical records suggests that the cases fall naturally into two great groups, namely, one including all those which terminated fatally, and a second embracing all those which ended in recovery. The fatal cases will be discussed first.

GROUP I - FATAL CASES

In the greater number of the fatal cases leucocytosis was present, though it usually manifested itself in a marked degree only after the appearance of the rash. Speaking generally, it may be said that the leucocytosis present in the fatal cases increased to a maximum at or just before the crisis, and declined thereafter, if death did not immediately supervene. In most of them there was a slight ante-mortem rise, but in two (Cases 5 and 9), this rise was very marked, as if the blood-forming organs had suddenly put forth a great and final effort, and it is remarkable that in none of the fatal cases were eosinophile corpuscles found at any time. This peculiarity is not limited to typhus, but is found in other diseases, e.g., pneumonia etc., and occurs apparently only in cases which eventually prove fatal (Becker - Deut. Med. Woch. 1900, Vol. 26). The number of red cells in all the fatal cases was higher than is usual in normal blood.

GROUP II - RECOVERIES

In this group the main facts of the blood examination correspond with those already detailed in connection with Group I. There was a gradual increase in the number of leucocytes from the beginning of the disease onwards, more marked after the appearance of the rash, until the maximum was reached by a rapid rise, either a day or two before, or coincidently with the crisis. After the crisis a sudden fall occurred, and the leucocytosis gradually declined during convalescence until the normal was reached.

With the supervention of inflammatory phenomena during convalescence, the leucocytosis may undergo a secondary rise, which, however, never exceeds, or even approaches, that which occurs at the crisis.

VARIETIES OF LEUCOCYTES PRESENT IN TYPHUS BLOOD

In addition to the facts furnished by the foregoing general considerations with reference to the condition of the red and white corpuscles, an analysis of the modifications undergone by the various leucocytes, both in number and character, reveals some features of interest. These are noted in connection with each type of cell in the following statement.

POLYMORPHO-NUCLEAR LEUCOCYTES

The polymorpho-nuclear neutrophile leucocytes arise, for the most part, in the bone marrow, and thence migrate into the blood stream. In response to the chemiotactic influence of various toxines, these cells are produced in greater numbers than usual, and being thrown into the peripheral circulation, a leucocytosis follows. The majority of febrile infectious diseases - pheumonia, erysipelas, diphtheria, septic conditions, acute rheumatism, etc., are accompanied by a leucocytosis of a greater or less degree. In this connection measles and uncomplicated enteric fever occupy a special position, as in these diseases the absolute number of white blood corpuscles is diminished, and this chiefly at the expense of the polymorpho-nuclear variety. These results, no doubt, depend upon the influence of the chemical products produced by the causative agent of the particular fever, and it is of interest to remember in this connection that such drugs as phenacetin etc. produce polymorpho-nuclear leucocytosis in man. This last has been observed experimentally by Rieder (Beitrage, Zur, Kenntniss der Leucocytose, 1892).

The polymorpho-nuclear cells, which are the most numerous of all the varieties of leucocytes in the normal blood, undergo in typhus fever, a marked relative increase, being frequently as high as from 80 to 90 per cent. of all the white cells present, and, in one or two instances observed, as high as 93 per cent. This relative in-

crease usually, but not always, corresponds with an absolute increase, and is practically the same in the fatal and non-fatal cases; that is to say, as regards the degree of leucocytosis, the fatal cases do not differ materially from the non-fatal cases.

Occasionally disintegrative or degenerative changes were noted in these cells, but these did not appear at any particular period in the course of the disease, nor could any special interpretation be placed upon these changes as they were not at all constant.

LARGE MONO-NUCLEAR CELLS

In most forms of leucocytosis the large mono-nuclear cells of the normal blood are not concerned in the increase. Indeed, in leucocytosis of high degree, their relative number may be lowered in consequence of the exclusive increase of the polymorpho-nuclear cells.

There exists some doubt not only as to the sources of formation of these cells, but also as to the manner in which they reach the circulation, for it appears that they do not react to chemiotactic influence in the way the polymorpho-nuclear cells do. Ehrlich inclines to the opinion that the large mono-nuclear leucocytes arise, for the most part, from the bone marrow. He found that in animals, from which the spleen had been removed, there was no alteration in their numbers, and there was no evidence of their formation in any of the other blood-forming tissues.

The occurrence of large mono-nuclear leucocytes in the blood of

typhus is constant, but the proportion constituted by them varies greatly, according as the case tends to recovery or to a fatal issue.

Although probably no diagnostic value can be placed on this phenomenon, it still remains a fact that in non-fatal cases, the relative proportion of these cells is greater than in fatal cases generally. In no case were these elements found to be absent from the blood, and they were present from beginning to end of the attack, though more abundant after the crisis.

LYMPHOCYTES

The lymphocytes of the blood are identical with those of the lymphatic glands in morphological character, staining properties, etc., and clinical experience points to the collections of lymphatic tissue throughout the body as being the origin of these corpuscles.

Lymphocytosis in comparison with other leucocytoses is comparatively rare, but it makes its appearance under certain conditions in which the lymphatic glandular tissue is in a state of congestion and over-stimulation. Many observers have advocated the view that the lymphocytes represent an early stage of development of the other white blood corpuscles, but it is difficult, however, to reconcile this theory with the observations of Ehrlich and others, who have noticed that, when extensive portions of the lymphatic glandular system are put out of action by new growths and similar causes, the number of lymphocytes in the peripheral circulation is considerably diminished. In acute infectious diseases lymphocytosis is rare, the

two most notable exceptions being whooping cough and smallpox, the blood of which is characterised by an increase in the number of lymphocytes.

An examination of the condition of these cells in typhus fever in the present series of cases shows that they are relatively diminished in numbers, in marked contrast to the polymorpho-nuclear variety. The decrease is usually both a relative and an absolute one, and is in marked contrast to the great increase in the polymorpho-nuclear cells. In both fatal and non-fatal cases this form of leucocyte appears to behave in the same manner. The greatest relative decrease in the number of these cells is represented by .4 per cent. In children, as one would naturally expect, the relative decrease of lymphocytes is less than in adults.

EOSINOPHILE CORPUSCLES

There is some diversity of opinion as to the origin of these cells. Ehrlich and his followers maintain that they are produced in the bone marrow, whilst others, as Shaffer (Cent. f. d. Med. Woch. Wissen 1891) and Gulland (Jour. of Path. and Bact. 1894) hold that they are derived from the thymus and lymphatic glands, as they have found them in these situations before their appearance in the marrow. Another method of production is indicated by Müller (Deut. Archiv. f. Klin. Med. 1891) who has observed active mitosis occurring in these cells. The supposition also that eosinophiles may be a further development or ripening of the polymorpho-nuclear leucocytes, has not

been entirely disproved, but, on the whole, the evidence seems to be against this explanation. Some observers have described a diminution in the number of eosinophiles in septic diseases, although Klein (Cent. f. m. - Med. 1899) publishes a case of hemorrhagic septicemia where eosinophiles appeared to the extent of 76 per cent. in the pleural exudate, and 40 per cent. in the blood. In this connection experimental leucocytosis in animals is of some interest. Kanthack found that, after the intravenous injection of a small quantity of sterile cultures of bacteria, an enormous leucocytosis sometimes occurred, mainly due to an increase in the number of eosinophiles (B. M. J., 1892), whilst though Neusser (Wein. Klin. Woch. 1892, No. 4) sometimes found in man an increase in the number of eosinophiles as the effect of various toxines, other observers have repeatedly found the leucocytosis, when present, to depend in the great majority of diseases, not on an increase in the number of eosinophiles, but upon an increase in the number of the polymorphonuclear variety.

Eosinophilia, though rare in septic diseases, has been observed in many other conditions, and more especially in bronchial diseases, cutaneous affections, and in certain diseases having their seat in the sympathetic system of nerves.

In the series of fatal cases of typhus recorded here, careful and repeated examination of films invariably failed to find eosinophile corpuscles at any period in the course of the disease. On the other hand they were constantly found in differentiated films taken from the non-fatal cases. They were not constant as regards time of appearance, for, though in some cases they were found only after the crisis, in the majority they were marked from the first count on-

wards.

In many infectious diseases there is, during the post-febrile period, a well marked eosinophile leucocytosis, which generally, however, rises to a moderate height only. In pneumonia Türk found a post-critical eosinophilia of 5.67%, and after rheumatism 9.37%, whilst Zappert found 20.34% in malaria on the day after the final attack.

No definite eosinophilia occurred in the typhus cases after the crisis, though, as has already been stated, a greater number of these cells was present during the period of convalescence than during any other stage of the disease. This phenomenon is illustrated on the charts.

Disintegrated eosinophiles were not common, although "burst" cells were occasionally met with.

With regard to the size of these cells, and of their granules, both were usually fairly constant, but at times a dwarf cell was noticed. No cell forms were observed in the differentiated blood films suggesting a transition between the coarsely granular poly-morpho-nuclear leucocytes and neutrophile eosinophiles, so that, if such a development of the one form into the other does occur, it must take place in the tissues, and not in the peripheral circulation.

MYELOCYTES

The importance of these cells and their significance, when they appear in the peripheral circulation, has been demonstrated by Muir (B. M. J., 1898), who pointed out that in grave inflammatory or infective conditions when the number of leucocytes falls, finely granular leucoblasts of the marrow - myelocytes - appeared in the blood, and he considers this to be a bad omen. Engel (Deut. Med. Woch., 1899) pointed out that in diphtheria, when these cells appear in large numbers, the case is unfavourable, and he found as many as 12% in some cases. In several other infectious diseases Türk (Blut. bei. Infect. Krauk 1898) found that a considerable number of these cells may appear accompanying polymorpho-nuclear leucocytosis, and other observers have recorded their presence in progressive pernicious anemia and leukemia. Although these cells resemble morphologically the polymorpho-nuclear leucocytes, on the one hand, and hyaline cells on the other, and have their origin in the bone marrow, their appearance in the peripheral circulation signifies some grave change influencing the cell producing function of the bone marrow.

In the present series of typhus cases, myelocytes were occasionally noted in the differentiated films, but so infrequently as to warrant their being disregarded in the percentage results.

In view of the observations just quoted, their scarcity is remarkable, but the appearances presented by the blood-forming organs, which are discussed later in this thesis, explain the absence of

these cells from the blood.

RED CORPUSCLES

The importance of the pathological changes which take place in the red blood corpuscles in certain general diseases is now fully recognised. Increase in the number of red corpuscles is not so common as diminution, but it is met with in certain febrile diseases as pneumonia, bubonic plague, etc., in which it is important to observe slight cyanosis is generally present.

It is a disputed point whether there is an actual over-production of red corpuscles in these cases, or whether the increase is only apparent and the result of vascular changes causing a tendency to an accumulation of a larger proportion of red cells in the blood of the peripheral vessels than in that supplying the various organs and deeper tissues.

Whatever the explanation may be, there is no doubt of the fact that an increase is met with in the diseases mentioned. The element of stasis must always be remembered, however, and allowances made. Indeed, many of the exceptionally high estimates reported in some cases of pneumonia may be explained by abnormality not of production but of distribution.

Many of the acute infectious fevers - enteric etc. - are accompanied by diminution in the number of red corpuscles, and, in some instances, by a marked anemia. Typhus fever, however, is an exception. This disease is essentially one in which cyanosis constitutes

a symptom which gradually becomes more marked as the disease progresses, and it may be, as already indicated, that the increase in the number of the red cells is due to this condition.

In nearly every case of the series recorded here there was an increase in the number of the red corpuscles at some stage of the disease. This increase became more marked near or at the time of crisis, and as convalescence became established, these cells gradually returned to an approximately normal number. In two cases (Case 3, Group I, and Case 2, Group II) examination of the fresh blood on the day when the crisis occurred, showed fragmentation or splitting up of many of the red blood corpuscles, some of them being split into two, and others into three or more parts. The explanation of this phenomenon is a matter of conjecture.

The question as to whether the increase in the number of red cells is due to an actual manufacture of new corpuscles, has already been alluded to, but there seems to be no reason to suppose that there is in typhus fever any unequal distribution of cells in favour of the periphery, such as is obviously the condition in ordinary cyanosis with stasis.

NUCLEATED RED CORPUSCLES

The clinical importance of nucleated red corpuscles has been demonstrated in many diseases, and especially in anemias. In various infective conditions Muir has pointed out their association with myelocytes in the peripheral circulation, and in the spleen. Three

kinds of nucleated red corpuscles are usually distinguished, viz., normoblasts, megaloblasts, and microblasts. The first is of the usual size of a red corpuscle; the second two to four times as large; and the last much smaller than the ordinary red blood cell. Occasionally these cells are found in normal blood. When they appear in large numbers, the condition is distinctly pathological, and then the preponderance of one variety or another possesses a certain diagnostic value.

The origin of the nucleated red blood corpuscles is the same as that of the ordinary non-nucleated cells - that is to say, they are derived from the bone marrow, where they can be seen in large numbers lining the wide capillary spaces.

In the series of typhus cases dealt with in this paper, nucleated red blood corpuscles were found only very occasionally. No special significance can be attached to their appearance in the blood, and it may be that their presence was merely accidental. The normoblastic form only was observed. The association of these cells in the blood of some infective conditions with myelocytes, to which Muir has alluded, receives negative confirmation in the condition of typhus blood, in which neither myelocytes nor nucleated red cells are abundant.

BLOOD PLATELETS

These elements of the blood were first described by Hayem who called attention to their special characteristic of running together into clumps or grape-like clusters.

Their presence is constant in normal blood, but the significance of their occurrence is still a matter of conjecture, although there is a tendency to associate them with the phenomena of coagulation. Muir (Journ. of Anat. and Phys. Vol. XXV, 1891) found a marked increase of the blood platelets in cases of chlorosis, whilst Denys (Revue: La Cellule, Vol V, pt. I) found a very marked diminution in two cases of purpura, and Ehrlich has examined cases in which they were wanting altogether.

In the blood of the typhus cases recorded here, blood platelets were always present, sometimes in large numbers. They were not observed in films stained with Ehrlich's triacid mixture, but were always well defined when Romanowsky's stain was employed. No marked difference was noted in the frequency of occurrence of these elements in the fatal and non-fatal cases respectively.

Having now discussed the various elements of the blood of which there is more or less accurate knowledge, there remain others of which there is no adequate description to be found in literature. These may be grouped into three classes:- 1. Cell debris; 2. Parasites; and 3. Hemoconia.

The earliest reference to these less known elements of the blood is to be found in a paper by Drs. Mott and Blore (B. M. J. 1883, "Micro-organisms in Typhus Fever"), who regarded them as micrococci. These observers describe the bodies thus, "We have examined the blood in twelve cases (of typhus fever) during the pyrexial stage, and in all moving organisms, like minute screws, have been seen. Occasionally their form can be made out, and we consider them

to be dumb-bell micro-cocci undergoing division. Often single cocci could be seen, and these were found to measure about half a micro-millimetre. In one case, there were large numbers in the blood after the fever had subsided; but, as a rule, they disappeared on convalescence."

The next observer to mention them was Doehle (Centralblat f. Allg. Path. w. Path. Anat., III, 150; Centralblat. f. Bakteriol. w. Parasit., XII, 906), who found them to be present in the blood of patients suffering from measles, scarlet fever, smallpox, and syphilis. He described them as small spheres (0.5 - 1 μ) which were either homogeneous, or contained a highly refractile nucleus surrounded by a clear zone. They showed movements which, in some instances, could be observed to be due to the action of a flagellum, four or five times the length of the body. Occasionally two spheres were enclosed in a common capsule. He also noticed granular and amoeboid elements (2.5 μ), and ill-defined rod-like protoplasmic bodies possessing small flagella.

Pfeiffer (Die Protozoen Als. Krankheitserrger, 1895) describes similar bodies with flagella which he found in the blood of patients suffering from variola and vaccinia.

The next descriptions are those of Müller and Reed. Müller, who gave to these elements the name of hemoconia (Centralblat. f. Allg. Path. w. Path. Anat., 1896), states that they are found in the blood as very small granule or cocci-like colourless corpuscles, highly refractive, with a very active molecular movement, which keep their shape under observation for a very long time without any special precautions. He found them in every normal blood in varying numbers, and was unable to stain them with osmic acid.

Various other observers have considered them as free granules of neutrophile or eosinophile leucocytes, or produced by fragmentation of the red blood corpuscles.

Observations made by myself on the blood of patients suffering from the diseases above mentioned, and on the blood of typhus patients, have demonstrated that there exists in the blood a number of forms which may be grouped into four divisions:-

1. Protoplasmic bodies containing a number of bright refractive points. There is no difficulty in demonstrating the origin of these as portions of neutrophile cells when stained with Biondi's fluid. They are observed frequently in blood where disintegration of corpuscles is common, as, for example, in hemorrhagic smallpox, but are not so frequently found in typhus fever.

2. Small round highly refractive bodies, .5 to 1 μ in diameter, and apparently motile.

3. Rod-like bodies, also apparently motile, $\frac{1}{2}$ to 2 μ in length.

4. Dumb-bell forms, 2 to 4 μ in length, and apparently motile.

With regard to the last three forms, it is probable that they belong to the same class, as they are all small, colourless, refractive bodies lying free in the blood plasma, and endowed with active tremulous movement. They vary in shape according to the position which they occupy, but for the most part appear as described in Class 2. They are never at rest, but dance about in an apparently aimless fashion, disappearing and reappearing with great rapidity as they pass out of focus, or come into view again.

Under certain optical conditions they appear to possess flagella, but it cannot be stated positively that these organs exist. It is interesting to note that these bodies are also found in the lymph from the early vesicles of smallpox.

Under no circumstances has success been attained in staining these elements, even in the lymph of the variola vesicle, where they exist in considerable numbers. They do not stain with osmic acid, or with Soudan red, our experience agreeing with that of Müller in this respect. Whether this is due to the fixing is difficult to say, but they have never been observed except in freshly drawn fluids. All modes of fixing - heat, Hermmann's solution, Fleming's solution, and corrosive sublimate, apparently destroy them, or at least cause them to disappear.

In typhus fever these bodies are constantly found in the freshly drawn blood. They are observed throughout the whole course of the disease, but appear in greater numbers during the first four or five days.

Apparently no prognostic significance can be attached to their presence as they are as frequently observed in fatal, as in non-fatal, cases.

There seems to be no doubt also that these bodies possess no etiological relationship with the disease, but, with regard to their abundance in many cases of typhus, the experience gained from the study of the cases recorded here tallies with that of Mott and Blore (B. M. J., 1883).

It has been suggested that they are derived from the disintegration or fragmentation of leucocytes or red blood corpuscles, but the fact that they do not stain is almost sufficient to negative this idea, and their mysterious disappearance during the process of fixing renders the collapse of the theory absolute.

An analysis of the observations detailed in the preceding charts and tables, and in the foregoing paragraphs, in which the various blood cells are dealt with, leads to the following conclusions:-

1. That typhus fever is always accompanied by leucocytosis, whether the attack be fatal or not.

2. That the character of the leucocytosis is practically the same in all cases, and corresponds with that found in certain of the other exanthemata, e.g., scarlet fever, inasmuch as it is the result mainly of an increase in the number of the polymorpho-nuclear cells.

3. That in the blood of fatal cases there are no eosinophile cells, whilst in non-fatal cases these corpuscles are always present.

4. In non-fatal cases there is occasionally a slight relative increase in the large mono-nuclear elements.

5. The red blood corpuscles are usually increased in number.

While bearing these general conclusions in mind, the full clinical significance of the observations can only be gauged after a careful and detailed analysis of the characters and numbers of the different groups of white cells, as well as of the conditions under which these are present.

Two cases (IV and VI, Group II) were admitted during the period of incubation, and on these observations were carried out during this stage. An examination of their charts shows a certain amount of febrile disturbance prior to the prodromal stage, followed by a period of 48 hours, during which the temperature remained normal, and this again was succeeded by a febrile excursion marking what must be regarded as onset of the true attack.

It will be noticed that, in both the cases, and accompanying

this preliminary temperature there was a certain degree of leucocytosis of the polymorpho-nuclear type, suggesting that the specific poison of the fever was already beginning to influence the hemogenic tissues. This is well seen in both, but better in Case 4 (Group II), an adult, than in Case 6 (Group II), a child of six months. It is known that very slight causes may lead to an increase of the leucocytes in the blood of a young child, but the leucocytosis of children is usually a lymphocytosis, and not a polymorpho-nuclear one, as in this case, a fact which is highly suggestive that the disturbance in the blood-forming organs is due to the influence of toxines.

Another point of interest is the relationship between the appearance of the eruption and the leucocytosis. In nearly all the cases observed, although the date of the first appearance of the eruption varied considerably, there was a distinct increase in the number of leucocytes on the days following its appearance. While this is of interest, yet the exact relationship between the first appearance of the rash and the leucocytosis is not obvious. Charts 4, 5, 7, and 9 (Group II) show this best.

Perhaps the most interesting phenomena indicated on the charts are those which group themselves around the crisis. In many of the cases a true crisis occurred, though in others a lysis terminated the attack, but in all cases observed the same phenomena as regards leucocytosis were present, that is to say, there was a gradually increasing leucocytosis up till one or two days before the crisis, when there was a sudden and rapid increase in the number of leucocytes. This increase, however, may occur on the day of crisis. A high grade leucocytosis is not maintained for any length of time,

for, in almost every case, a fall, as striking as the preceding rise, occurs on the following day, and thenceforward the number of leucocytes declines with the temperature.

The normal number of leucocytes in the blood, however, is seldom reached until convalescence has become fully established. In Cases 2, 4, and 10 (Group II), this delay in reaching the normal may be accounted for by the fact that, in these three cases, bronchial catarrh persisted for a few days after the crisis had occurred, but, in none of the other cases, was this explanation available. In Case 9 (Group II), however, there was a thrombosis of one of the smaller veins of the left leg, and this possibly accounts for the irregular leucocytosis maintained after the crisis.

Regarding the question as to the presence of a constant ante-critical rise, exception must be made of those cases in which the illness terminated fatally, though, even in these, there is evidence to show that leucocytes are thrown into the blood at this period in abnormally large numbers; in fact, in greater numbers than at any other period of the illness except that which immediately precedes death.

As already stated, the leucocytosis is mainly a polymorpho-nuclear one, but in the non-fatal cases there is also to a limited extent a leucocytosis due to an increase in the large mono-nuclear cells, which becomes more pronounced in the majority of cases after the crisis, and is perceptible during the first few days of convalescence, until the normal proportions of the different leucocytes has been restored.

From the point of view of diagnosis the leucocytosis of typhus

fever is of some importance, inasmuch as it affords a basis for differentiating between this disease and enteric fever, in which there is no leucocytosis, but rather a diminution in the number of leucocytes.

It has been shown in the earlier part of this thesis that leucocytosis is present in typhus fever, even at the beginning, and certainly always after the appearance of the rash, so that a doubtful case giving a distinct leucocytosis cannot be regarded as enteric fever, unless this latter be complicated by the presence of some inflammatory condition.

This is of interest in view of the fact that, in typhus fever, a positive widal reaction is sometimes obtained, but this point will be dealt with more in detail in the Appendix.

In enteric fever there is a steady and progressive decrease in the number of red blood corpuscles, becoming more and more marked as the disease advances, whilst in typhus fever it has been shown that the exact opposite occurs, namely, that there is rather an increase in the number of red cells as the disease progresses towards the crisis. Again, in enteric fever, there is always, in the absence of inflammatory complications, a sub-normal number of leucocytes, which is most marked after the first week of fever. In typhus, on the other hand, there is always a certain degree of leucocytosis, which generally becomes more marked after the first week of pyrexia.

In these particulars, there is such absolute and complete difference that the one disease should never be mistaken for the other although there is some apparent similarity in the manner in which the large mono-nuclear and eosinophile cells behave.

While the diagnostic significance of the condition of the blood in typhus fever has been shown to be of importance in differentiating between that disease and enteric fever, the same cannot be said regarding its significance in pneumonia and bubonic plague. Of the more common diseases pneumonia is perhaps the one most likely to be confused with typhus fever, for the onset and course of the pyrexia are so similar in both, that in the absence of rash on the one hand, and of physical signs in the lungs on the other, confusion is not unlikely to take place.

In distinguishing between these two diseases, the blood unfortunately offers but little help. In pneumonia "the red cells are either normal or slightly diminished during the active stages of the fever, but polycythemia may occur" (Da Costa), so that little diagnostic value should be attached to a consideration of the number of these corpuscles, seeing that in typhus fever they are either normal or somewhat increased during the active stages of the disease. The leucocytes, too, offer no help in diagnosis, as in the great majority of cases of pneumonia "a well-marked leucocytosis develops at or soon after the time of the initial chill, and persists until shortly after the temperature has fallen to normal" (Da Costa).

The same phenomenon occurs in typhus fever, so that differentiation between the two diseases by examination of the blood is almost impossible.

The leucocytosis in both is of the polymorpho-nuclear type.

In cases of pneumonia terminating by crisis, the leucocytes begin to diminish either a short time before or after the temperature commences to decline, the normal being reached in a proportion of the cases about a week after the temperature has dropped. This is

exactly what occurs in typhus fever, but, whereas it is stated that in about half of all cases of pneumonia, whether ending by crisis or by lysis, the maximum of leucocytes is attained during the period of temperature decline, in typhus it is not so, the maximum in this disease being attained almost invariably before the decline of temperature commences.

Attention has already been called to the similarity in the behaviour of the eosinophiles in pneumonia and typhus fever. In pneumonia the proportion of eosinophiles is much reduced, and frequently these cells are entirely wanting. This is regarded as an unfavourable sign by Becker (Deut. Med. Woch., 1900, Vol. 26), who states that he has always found them absent in fatal cases.

These remarks apply with equal force to typhus fever, in which a fatal prognosis seems to be warranted if the eosinophiles are absent throughout the attack.

Influenza is another disease likely to be confused with typhus on account of the similarity of the earlier symptoms. Here, on the other hand, an examination of the blood forms a ready means of excluding typhus, in view of the fact that influenza is one of the small group of febrile diseases in which leucocytosis is absent.

With regard to bubonic plague, although this disease is seldom likely to be mistaken for typhus because of its rarity in this country, it is interesting to find that the blood conditions are very similar, and afford little or no assistance in framing a diagnosis.

In plague the red blood corpuscles are always decidedly above the normal, a count as high as 8,190,000 having been obtained in one case. The same thing occurs in typhus fever, a red blood count be-

low the normal being the exception.

The leucocytes too in both diseases are markedly increased, and in both it is a polymorpho-nuclear leucocytosis.

It is stated that in plague the eosinophiles are absent, as in typhus, but no mention is made as to whether they are absent in all cases, or as in typhus, in fatal cases only.

In many respects, therefore, the blood of the two diseases presents similar characteristics, and an examination of that fluid alone would give little or no help in arriving at a diagnosis.

As regards prognosis little can be said concerning the general leucocytosis of typhus fever, but one or two points are brought out by differentiation of the cells, which may assist in forecasting the result of a case.

The fact that in fatal cases no eosinophile corpuscles are found has been already alluded to, and would seem to indicate that we may look for a favourable termination in any case in which these corpuscles are present throughout, especially if present in some numbers and before the crisis. If no corpuscles of the eosinophile type are found, it does not necessarily mean that the issue of the case will be fatal, but such a case must be looked upon as grave, and a certain amount of reserve maintained as regards prognosis. In non-fatal cases there is an increase in the number of the large mono-nuclear forms of leucocytes, so that this also may be taken as an indication of a favourable issue, but merely as an indication, seeing that these leucocytes come more into evidence during the first few days of convalescence.

The degree of leucocytosis in general appears to have little or no prognostic value.

TYPHUS BLOOD

SPECIFIC GRAVITY AND HEMOGLOBIN

The specific gravity of the blood is considered to be of importance, as the density of this fluid is said to afford a measure of the number of red blood corpuscles present, and of their hemoglobin equivalent.

In the last few years two methods of determining the specific gravity have come into use which require only a small quantity of material, and do not appear to be too complicated for practical purposes. One of these methods, which has been worked out by R. Schmaltz, depends upon the accurate weighing of small quantities of blood in capillary tubes. The second method is that of Hammerschlag. In this a mixture of chloroform and benzol is so arranged that, when a drop of blood is thrown into it, it floats indifferently in any part of the fluid, which is contained in a moderately deep and narrow vessel. Under these circumstances the specific gravity of the blood must be the same as that of the fluid in which it floats. Great accuracy can hardly be expected from this method, as errors may arise from changes in the blood drop during and after its transfer to the mixture, from evaporation, from the escape of gases, from the inclosure or adherence of minute air bubbles, and perhaps also from the possible action of chloroform and benzine upon the blood,

an action which is at present unknown. Practically, in carrying out the test, it is found that the behaviour of the drop varies for reasons which are not clear, some rising and others falling in the same mixture. Hammerschlag's method was that employed in the following cases, but, instead of using a hydrometer, the mixture in which the blood drop remained stationary was accurately weighed in a specific gravity bottle, in order to eliminate errors arising from the use of an instrument in a fluid, the surface tension of which is entirely different from that for which the instrument is graduated.

The estimation of the amount of hemoglobin in the blood of certain general diseases is also of considerable importance, especially in connection with the various anemias. Various methods of estimation are employed, but that which seems to find most favour in this country is the colorimetric one, that is, the method by which a drop of blood is mixed with a certain fluid and compared with a standard colour index. This method necessitates careful and delicate manipulation, and is only relatively correct as colour and transparency are both modified by dilution.

Another procedure which has gained some favour is to calculate the amount of hemoglobin from the specific gravity. The specific gravity is taken according to Hammerschlag's method, and the amount of hemoglobin calculated from a table drawn up by him. This method, however, is somewhat crude, and is only useful in cases where absolute accuracy is not important. In order to obtain complete accuracy, an instrument has been devised by Dr. Albert Henocque of Paris. It is called the "Hematoscope", and is used in conjunction with the spectroscope. It consists of two glass slides of unequal size, the

smaller of which is superimposed on the other in such a fashion that while they are in contact at one extremity, they provide a prismatic capillary space at the other. The position of the slides is assured by means of two clasps supported by the lower slide, and within these the upper slide is introduced. A graduated scale is engraved on the lower glass slide running from 0 to 60 millimetres. It thus happens that, when a drop of blood is introduced between the two slides, a layer of blood is formed by capillarity, of which the thickness varies from left to right. The tint of the blood also varies according to the thickness of the layer, and the amount of hemoglobin present; the point on the scale at which the two absorption bands characteristic of oxyhemoglobin become of equal intensity in the spectrum is noted, and the reading compared with a table which is provided with the instrument. Thus a reading of 13 millimetres is equivalent to 15% of hemoglobin in the blood, 14 millimetres to 14%, 15 millimetres to 13% etc.

Each instrument is verified before being issued, so that accuracy is guaranteed, and with a little practice the operation becomes very easy.

The last method was the one employed in determining the amount of hemoglobin in the blood of the following cases, and as the enumeration of the red blood corpuscles is of importance in this connection, these cells were counted at the same time as the hemoglobin was estimated.

In order to give a clear idea of the results of the investigation, these have been graphically depicted on the accompanying charts, and also set forth in tabulated figures.

Four cases in all were investigated, and a very short clinical

history of these will suffice to demonstrate their nature.

CASE I. The first case was that of George F., aet. 52, who was admitted to hospital on 7th April 1904, his ninth day of illness. His temperature was 102.4° F., pulse rate 102, and respirations 44 per minute. A profuse and typical typhus rash was present. On the fourteenth day of illness the temperature became normal, and convalescence began.

The enumeration of the red blood corpuscles and the estimation of the specific gravity and hemoglobin was begun on the day after admission, and continued daily thereafter at the same hour until convalescence was fully established.

The results are given in the following table and shown on the accompanying chart.

Date Apl.	Day of Illness	Temperature F. M	E	Red Cells	Percentage of Hemoglobin	Specific Gravity
8	10	100.4	100.6	6,100,000	15	1049
10	12	99.4	102.6	5,300,000	15	1045
11	13	99.2	100.4	5,700,000	15	1046
12	14	99.8	99.8	5,450,000	14	1048
13	15	98	99.2	5,900,000	14	1049
14	16	97.8	98.8	6,000,000	14	1048.5
15	17	98.4	98	5,650,000	14	1049.5
17	19	98	98.4	5,150,000	14	1049.5
24	26	98	97.8	5,000,000	13	1045
May 21	50	98	98	4,840,000	12.5	1040

CASE II. The second case was that of John McM., aet. 10, who was admitted to hospital on 28th June 1904, his fifth day of ill-

EXPLANATION OF CHART

Red Blood Corpuscles	in Red
Hemoglobin - percentage of the whole blood	in Green
Specific Gravity	in Violet
Temperature	in Black

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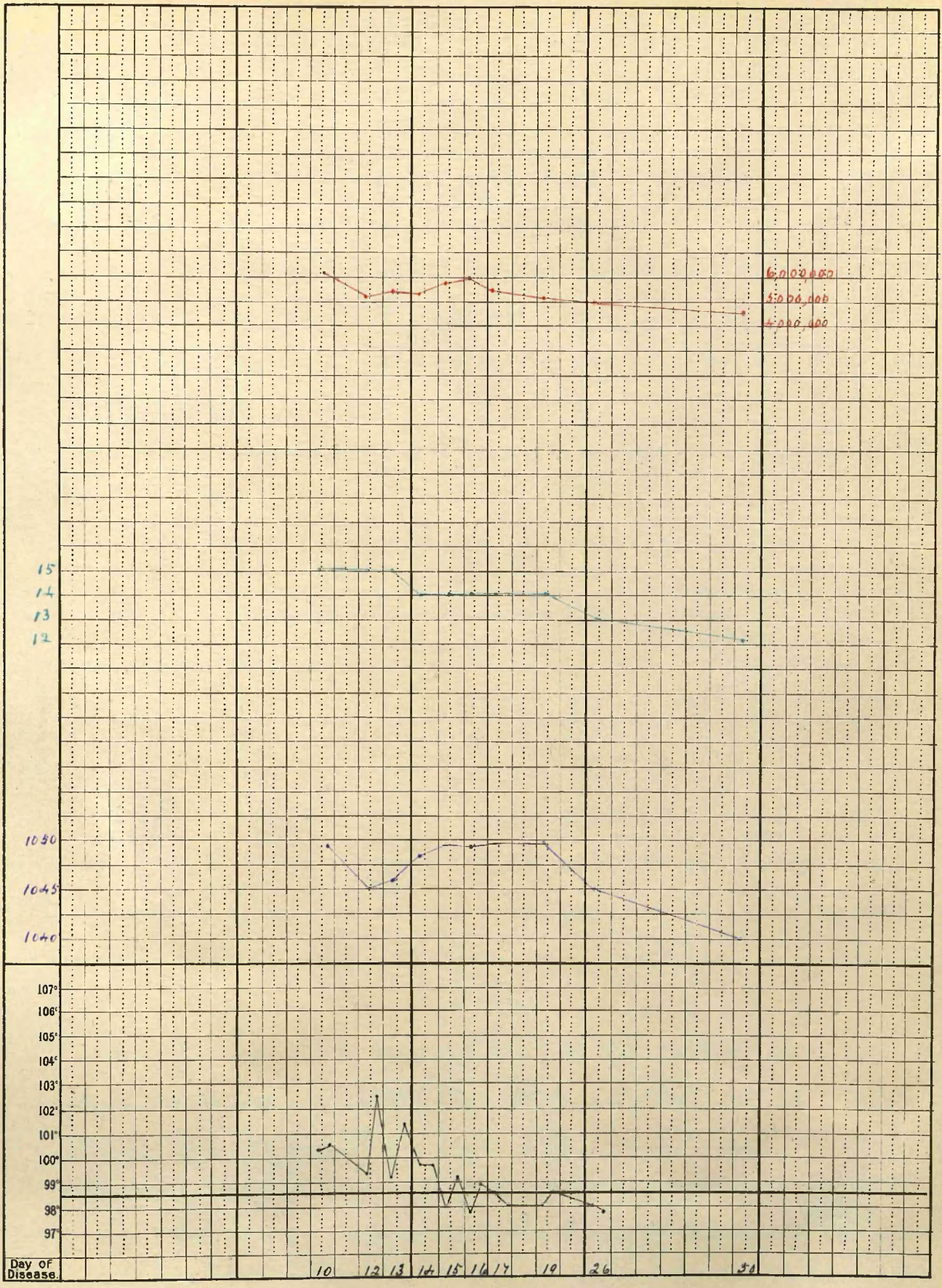
Chart I.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Day of Disease.
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ness. The temperature was 103.4° F., pulse rate 120, and respirations 40 per minute. A typical typhus rash in the early stage was present. The attack was a very sharp one, and the crisis, which occurred on the fourteenth and fifteenth days of illness, was followed by a slight irregular pyrexia for a few days.

The estimation of the hemoglobin and specific gravity, and the enumeration of the red blood corpuscles were commenced on the ninth day of illness, and continued thereafter every second day during the acute stage of the disease.

The results are given below in a table, and on the accompanying chart:-

Date July	Day of Illness	Temperature F. M	E	Red Cells	Percentage of Hemoglobin	Specific Gravity
2	9	104	104.8	5,576,000	16	1049
3	10	103.6	102.4	6,130,000	15.5	1044
4	11	102.2	102.2	4,600,000	15.5	1044
5	12	101.8	102	5,090,000	15.5	1043
6	13	101.2	102.2			
7	14	101.2	103	4,690,000	14.5	1040
8	15	98.8	100.8			
9	16	98.4	100.2	5,041,000	16	1046
10	17	98.4	100			
11	18	98.4	99	4,640,000	14	1044

CASE III. The third case was that of Maggie McM., aet. 8, who was admitted on 2nd July 1904, that being her fifth day of illness. Her temperature was 104.2° F., pulse rate 112, and respirations 32 per minute. A typical typhus rash was present, and the disease followed a natural course, the temperature becoming normal on the six-

EXPLANATION OF CHART

Red Blood Corpuscles	in Red
Hemoglobin - percentage of the whole blood	in Green
Specific Gravity	in Violet
Temperature	in Black

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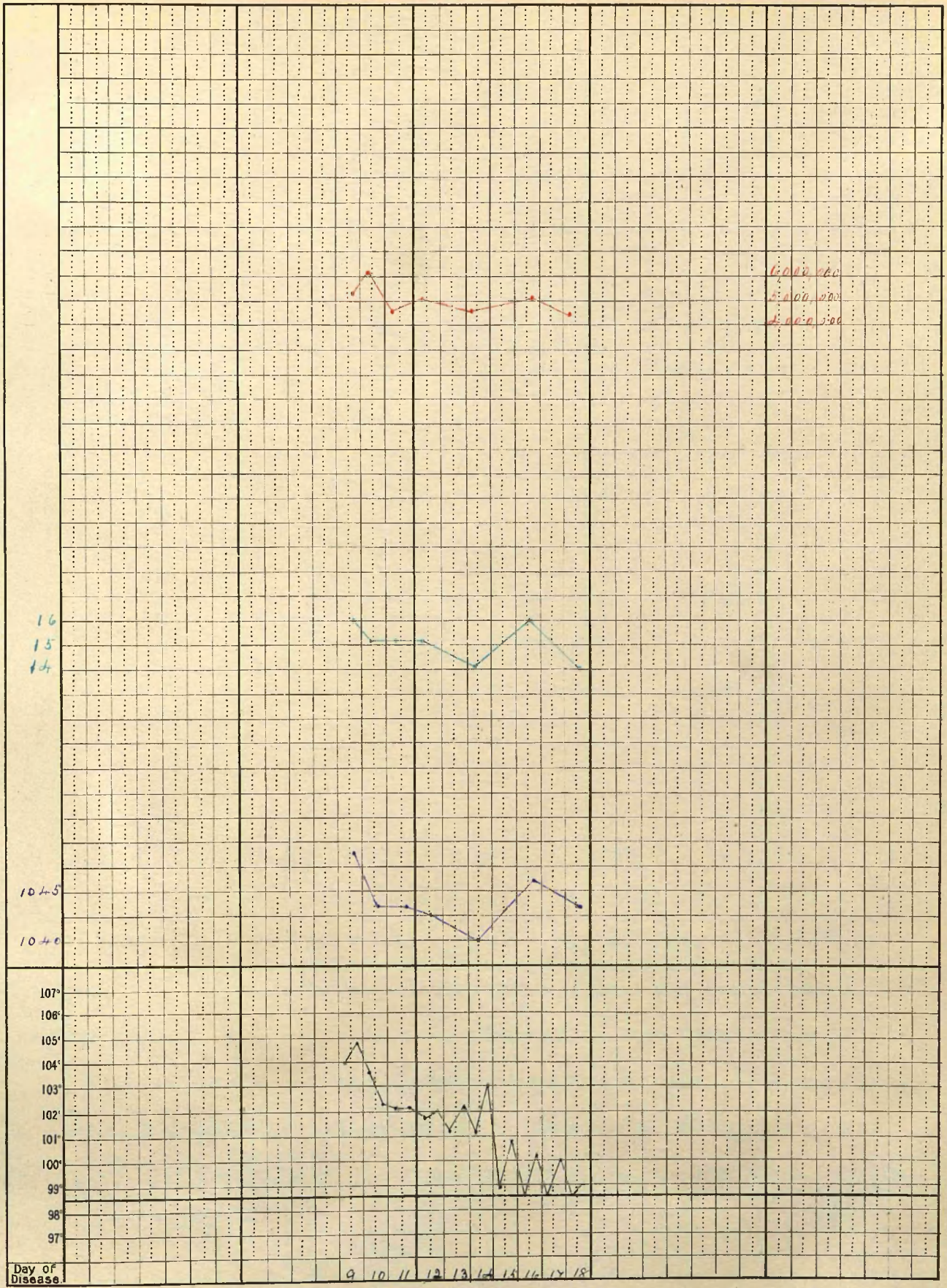
Chart II.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Day of Disease.
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teenth day of illness.

In this case the amount of hemoglobin, with the specific gravity, was estimated, and the red blood corpuscles counted every second day during the acute stage of the fever; the results are given below in tabular form, and graphically shown on the accompanying chart:-

Date July	Day of Illness	Temperature F. M	E	Red Cells	Percentage of Hemoglobin	Specific Gravity
2	5		104.2	5,750,000	15.5	1047
3	6	103	104	5,360,000	16	1048
4	7	103	104			
5	8	103.6	103.8	4,810,000	16	1043
6	9	103.4	104			
7	10	103	103.2	5,450,000	16	1043
8	11	101.8	103			
9	12	102.8	103	5,780,000	16	1041
10	13	102.2	103.4			
11	14	99.6	101	5,230,000	14	1038
12	15	100	100			
13	16	98.2	98.8	5,000,000	14	1040
14	17	98	97.6			

CASE IV. The last case was that of Rose C., aet. 5, who was admitted to hospital on 4th July 1904, her ninth day of illness. The temperature was 103.6° F., pulse rate 120, and respirations 36 per minute. On the fourteenth day of illness the temperature had become normal, and convalescence thereafter was uninterrupted.

The red blood corpuscles were enumerated, and the hemoglobin and specific gravity estimated every second day during the acute stage of the fever, and the results are shown in the accompanying chart and table:-

EXPLANATION OF CHART

Red Blood Corpuscles	in Red
Hemoglobin - percentage of the whole blood	in Green
Specific Gravity	in Violet
Temperature	in Black

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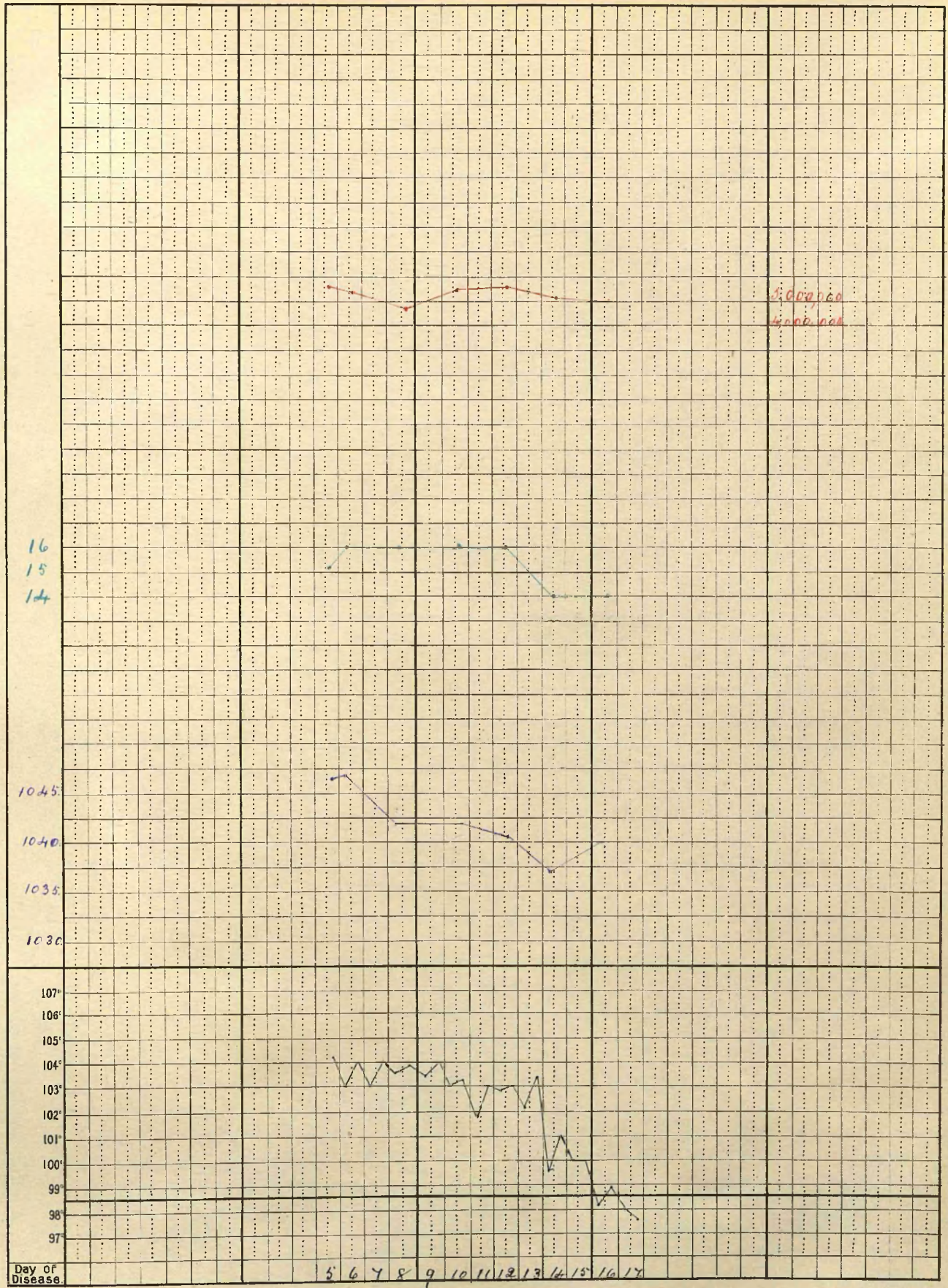
Chart III.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Day of Disease.
5 6 7 8 9 10 11 12 13 14 15 16 17

EXPLANATION OF CHART

Red Blood Corpuscles	in Red
Hemoglobin - percentage of the whole blood	in Green
Specific Gravity	in Violet
Temperature	in Black

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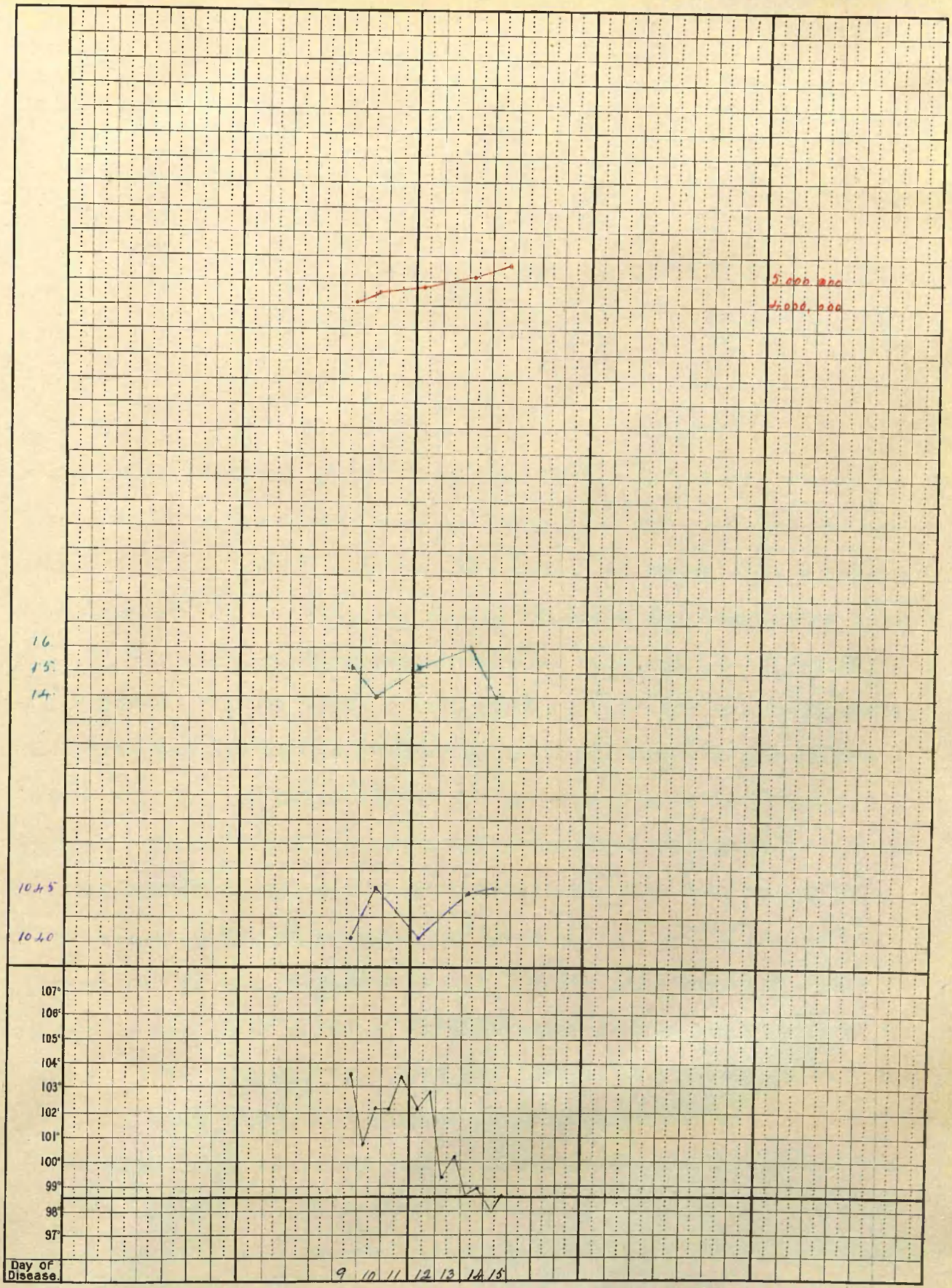
Chart IV.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Day of Disease.
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Date July	Day of Illness	Temperature F. M	E	Red Cells	Percentage of Hemoglobin	Specific Gravity
4	9		103.6	4,280,000	15.5	1041
5	10	100.8	102.2	4,830,000	14	1046
6	11	102.2	103.4			
7	12	102.2	102.8	4,980,000	15.5	1041
8	13	99.4	100.2			
9	14	98.4	98.8	5,090,000	16	1045
10	15	98	98.4	5,880,000	14	1046

A consideration of the foregoing tables and charts shows that the hemoglobin percentage is high throughout the whole of the acute stage of typhus fever, and that the amount of hemoglobin corresponds to a limited degree, with the number of red blood corpuscles present.

If the standard hemoglobin value be fixed at 14-15% of the whole blood, then it will be seen that in Case III the hemoglobin was in excess during the greater part of the acute stage of the fever, and that in Cases II and IV, an excess also was recorded on various occasions. The highest value obtained in any case was 16%, and the lowest 12.5%, whilst the average for the four cases is approximately 14.7%, or practically normal.

As far as can be judged from the cases here recorded there is little or no relation between the temperature and the amount of hemoglobin. After the occurrence of the crisis, the amount of hemoglobin gradually diminishes, and becomes normal, or as in Case I, somewhat under normal when convalescence is thoroughly established.

The specific gravity of the blood in typhus, as will be seen from a consideration of the tables and charts, is considerably lower

than that which is given for normal blood. This seems strange, considering that the red corpuscles and hemoglobin are higher than normal. If the various sources of error, already mentioned, be taken into consideration, there still remains a considerable difference, and the only manner in which this can be accounted for is by a very great diminution in the salts of the plasma. This explanation is difficult of verification, and is merely suggested as being the most probable.

ETIOLOGY

The specific cause of typhus fever is still unknown, so that it may be of some interest to compare this disease with others which resemble it as regards leucocytosis, in order to arrive, if possible, at some conclusion with respect to what kind of organism may be expected to be the most probable cause of the disease. This object has been the aim of many researches, and many observers have described what, in their opinion, was the true organism of typhus fever, but, up to the present time, none of them have gained complete recognition.

The two diseases which resemble typhus fever most closely in their leucocytosis are pneumonia and acute rheumatic fever. A comparison has already been drawn between the leucocytosis of typhus and that of pneumonia, so that it is only necessary to recall the similarity in almost every respect of the blood of these two diseases. As to acute rheumatic fever there is also a great resemblance

in the blood as regards leucocytes to that of typhus. The leucocytosis in rheumatic fever as in typhus is a polymorpho-nuclear one, and is always found during the acute stage of the disease, whilst in favourable cases eosinophile corpuscles are found during the acute stage, and are always present in greater numbers during convalescence.

Here, then, are two diseases, the leucocytosis of which resemble that of typhus fever, and one of which - pneumonia - bears a marked resemblance to that disease in many other respects, which are each caused by a certain specific micro-organism; in the case of pneumonia this micro-organism is a well-known diplococcus (Fraenkels), and in the case of rheumatic fever a diplococcus (Triboulets) is also described. Arguing from these facts, is there not a strong presumption that the specific organism of typhus fever - granting that there is one - may also be of the nature of a diplococcus?

Some observers, notably Balfour and Porter (Edin. Med. Journ., 1899, Vol. VI), have described a diplococcus in the blood of patients suffering from typhus fever, but their observations are open to much doubt, and the organism described by them is, in all probability, the substance known as hemoconia: this point has already been alluded to in the chapter on hemoconia, and therefore need not be discussed again.

A paper of interest bearing upon the etiology of typhus fever was recently published by Dr. Emil Gotschlich entitled "Uber protozoën Befunde (Apiosoma) im Blute von Flecktyphus-Kranken" in the Deutsche Medicinische Wochenschrift, 7th May 1903 (No. 19). In this paper the author describes a parasite which he claims to be that of typhus fever, and which he says is identical with Apiosoma. He des-

cribes the parasite thus, "The parasite appears in the interior of the red blood corpuscles (endoglobular form), and also free in the blood stream (two forms, cysts and flagellated bodies). The staining of the endoglobular form is well shown by diluted borax methylene blue. In order to stain the extraglobular form, use undiluted Ziehls Carbol Fuchsin for a few minutes, and then wash with water.

1. Endoglobular form - This form is chiefly pear-shaped, and varies in size from 1 u. to half the diameter of a red blood corpuscle; often only one pear-shaped body is found in a red corpuscle, seldom are two met with. Sometimes ameboid parasites with short thick processes are met with. Finally there are rod forms in which the chromatin shows a bi-polar arrangement: the border of the parasite is smooth and regular, and is generally more deeply stained than the interior. The interior, when stained with simple borax methylene blue, shows little round granules which stain deeply. When stained by Romanowsky's method, these granules appear red in the blue body of the parasite. In the pear-shaped forms there is at times a distinct grouping of the chromatin at both ends. In the youngest round forms the chromatin often shows the appearance of an open ring at the side. The whole parasite is at times surrounded by a distinct unstained ring. In the living unstained condition the parasite shows quite distinct active motility. In the little rod forms one has the impression of a little bacillus diving and rising in the interior of the blood corpuscle. The larger pear-shaped forms push against the wall of the red corpuscle, and bulge it out so as to alter its shape considerably. At times the completely infected blood corpuscle is in active tremulous movement without chang-

ing position - in marked contrast to the motionless normal ones in the neighbourhood.

In the fresh blood I have not seen the bodies which Dr. Gotschlich describes, but in film preparations stained in the manner he advises, I have observed bodies which are similar to those he mentions, although I have never been able to note the amount of detail which he states can be made out. These bodies which he describes, and which he calls the parasite, appear to be merely portions of the red blood corpuscles which have undergone degenerative changes, and which are often seen, not only in the blood of typhus, but in that of other infectious diseases, as variola etc. It is very striking that Dr. Gotschlich's description of his parasite corresponds exactly in many details with the description of endoglobular degeneration of the red blood corpuscles described in "Da Costa", which I shall quote shortly in order to show the similarity. "Loss of colour by the erythrocytes which progresses hand in hand with alterations in their size and shape, and other structural changes is regarded as a degenerative process of purely endoglobular nature. The discolouration may commence in <u>one or more spots</u>, or it may equally involve the whole surface of the corpuscle, beginning at its centre and spreading progressively towards its periphery. Clear hyaline areas of <u>oval</u>, <u>round</u>, or <u>elongated</u> shape appear within the stroma, in some instances sharply contrasting with the relatively dark colour of the hemoglobin, but, in other instances, imperceptibly blending with the tint of the surrounding cell body. The <u>active motility</u> of these decolourized spots must be carefully distinguished from the ameboid movements of the young malarial parasite." Then again, "Fragmenta-

tion of the delicate rim of colouring matter may occur, in event of which a number of independent rod-like bits of stroma are found. The decolourized area is not always symmetrical, so that frequently various bizarre designs may be observed. It has been determined that, in the dried blood film, these areas of decolouration show a decided affinity for basic stains such as methylene blue and thionin."

From the above description it will be seen that in corpuscular degeneration forms similar to those described by Dr. Gotschlich are often observed, that these forms are best shown by the stain which he employs (methylene blue), and that the motility upon which he lays stress is merely the usual phenomenon manifested by degenerated corpuscular elements.

Dr. Gotschlich states that his parasite is a form of Apiosoma. Now it is well known that Apiosoma and similar parasites occur only in these diseases in which there is great destruction of the red blood corpuscles. In texas fever, for example, the destruction is enormous; the number of red blood corpuscles has been known to sink from the normal (8,000,000 to 9,000,000 per c.mm.) to 31,000 on the second day. This destruction, too, is evidenced by marked hemoglobinuria.

In typhus fever, however, there is no such evidence of destruction of the red blood corpuscles; there is no blood in the urine, and it has already been shown that the red cells are not only not diminished, but rather increased in number in the peripheral circulation. This seems to be almost conclusive evidence against Dr. Gotschlich's parasite being that of typhus fever.

In consideration of these facts, the etiology of typhus fever

must still be held to be incompletely known, and, though the resemblance in the leucocytosis of that disease with other diplococcal diseases, as those mentioned, is suggestive, it may be that there is nothing more than a coincidence in the similarity.

In

THE BLOOD-FORMING ORGANS

In

TYPHUS FEVER

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ON THE CHANGES

in

THE BLOOD-FORMING ORGANS

in

TYPHUS FEVER

DESCRIPTION OF PLATE IV

Section of Bone Marrow from Case No. V showing ordinary marrow cells, and two capillary spaces filled with blood.

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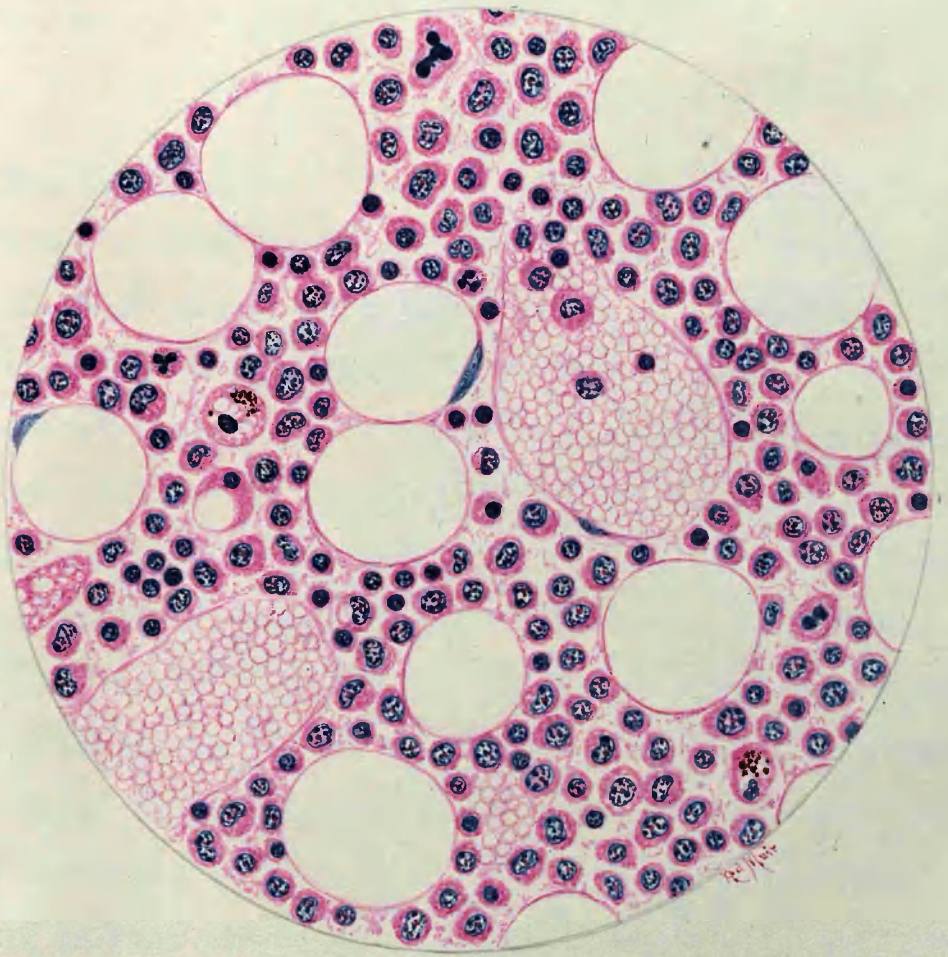

ON THE CHANGES IN THE BLOOD-FORMING ORGANS IN TYPHUS FEVER

The importance of the leucocytes in diseased conditions has been clearly established by exhaustive investigation on the behaviour of these cells, both with regard to their power of intra-cellular digestion or phagocytosis, and their power of producing and emitting certain bactericidal substances, exercising antagonistic influence upon pathogenic organisms. The behaviour of these cells in abnormal conditions gives some indication as to their functions in the economy of the organism in which they are present, but, in order to arrive at any definite conclusion concerning the laws which govern their production, it is necessary to compare and contrast the changes which occur in the tissues responsible for leucocyte production with those occurring in the white cells present in the blood.

It is well known that blood cell multiplication occurs in certain definite tissues which have some special relation to the blood and lymph streams, and that apart from these special situations leucocyte or other blood cell proliferation is comparatively rare.

Until comparatively recent years the spleen and lymphatic glands were regarded as the only organs concerned in the manufacture of blood corpuscles. Then came the discovery that red blood corpuscles were produced in the bone marrow, and later it was fully established by the researches of Ehrlich and others that the bone marrow was also

concerned in, and had as one of its principal functions, the production and multiplication of leucocytes. This tissue, therefore, is regarded as the principal manufactory of the polymorpho-nuclear corpuscles of the blood, and as its vascular arrangements are admirably adapted to the passage of large numbers of these cells into the blood stream in a short time, it is also regarded as the tissue mainly concerned in the production of leucocytosis. Ehrlich has always insisted on this, and his results have been abundantly verified by other observers. Because of this function of leucocyte production, Ehrlich regards the bone marrow as "a protective organ", evidently referring to the number of cells produced by it, and not to any special function of these cells as phagocytes: indeed, phagocytosis appears to be merely a secondary and subsidiary function of the marrow. In this respect it is quite unlike the spleen of which phagocytosis appears to be one of the main functions.

Bone marrow is thus principally a manufacturing or formative tissue, and the cells which it produces, and throws into the circulation, consist of red blood corpuscles and granular leucocytes.

Lymphoid or glandular tissue is another of the formative tissues, the corpuscles which are manufactured there being called lymphocytes. This tissue is represented by the various lymphatic glands throughout the body, by the Malpighian bodies of the spleen, etc. The vascular arrangements of lymphoid tissue are different from those of the bone marrow, although, like the marrow, this is essentially a formative tissue. There are no wide capillary spaces into which the cells can be rapidly poured, but the glandular tissue is surrounded by sinuses and lymph spaces, so that it would appear

that the lymphocytes do not reach the blood directly but by some circuitous route.

In the spleen the pulp is in close relation to the circulating blood, and this organ, like the lymphoid gland, appears to be peculiarly adapted for the detention of abnormal substances. The mononuclear cells of the lymphatic glands and of the spleen are very similar, and possess marked phagocytic properties towards both red and white corpuscles.

Although it has not been proved conclusively that polymorphonuclear leucocyte formation takes place normally in the spleen or lymph tissue, it has been shown that proliferation does occur under certain pathological conditions, the result of some definite local irritation or disturbance, as for example in bubonic plague.

Bearing in mind the above facts with regard to the importance of the different blood-forming organs in the production of leucocytosis, portions of each of these organs were taken post mortem, and it is now proposed to detail the results of the examination of these specimens.

The tissues from six cases were examined. From five of these, samples of bone marrow were taken, from three, samples of the inguinal glands, and in every case the tissue of the spleen was investigated. Film preparations of bone marrow were made, and portions of the marrow expressed from the rib were hardened in a fixing solution composed of formaline and alcohol, and used for section cutting. The films were allowed to dry in the air, and thereafter were fixed by heat. Film preparations were also made from the spleen, and for section cutting portions of that organ and of lymphatic glands were

preserved in absolute alcohol.

For section cutting the specimens were fixed as above described, embedded and cut in paraffin. For the examination of the marrow, that from the rib was selected in every case, and although the structural relations are necessarily altered by the pressure to which it is subjected in order to express it from the bone, the relative proportion of its cells remains undisturbed.

The sections proved in every way more satisfactory than the film preparations. Various stains were employed, the principal ones being Ehrlich's triacid stain, Romanowsky's stain, and Unna's Polychrome Methylene Blue with tannic acid fuchsin. With the last two stains the details of the nucleus were better seen, but Ehrlich's stain gave good general results.

CASE I. The first case is that of the child, Matilda A. (Case No. 3), who died on her nineteenth day of illness.

Specimens of spleen and lymphatic gland only of this case were kept. The spleen was enlarged and hyperemic, but of fairly firm consistence. The Malpighian bodies were prominent. Microscopic examination showed much cellular hyperplasia both in the pulp and in the Malpighian bodies. These cells were mainly of the small mononuclear variety with deeply staining nuclei, associated with a certain proportion of endothelial cells. The number of red corpuscles was greatly diminished.

One of the most striking features was the extent of the phagocytic action as judged by the large number of cells within which were present broken down or fragmented leucocytes, and debased red

corpuscles. Around the sinuses the phagocytes were larger, and there the process of phagocytosis, especially of the red cells, was more marked than elsewhere. The inclusion of fragmented leucocytes was most marked in the cells of the pulp. Polymorpho-nuclear leucocytes were present in comparatively small numbers only, and most of them showed signs of disintegration. Giant cells were exceedingly rare, and many sections were examined before any of these were discovered, and although careful search was made for myelocytes, none were observed. No bacteria were present, and mitosis was not observed in any of the splenic cells.

The lymphatic glands throughout the body were not enlarged.

Microscopic examination failed to reveal anything strikingly abnormal, although a certain degree of hyperplasia existed. The cells were mainly lymphocytes. Other cells which were larger and contained a nucleus of considerable size and abundant protoplasm were present. These larger cells are, in all probability, of endothelial origin as they were distinctly more numerous in the neighbourhood of the lymph spaces.

No polymorpho-nuclear leucocytes were observed, and no evidence of phagocytosis was detected. No bacteria, eosinophile corpuscles, nor cellular debris were found.

CASE II. The next case is that of Theresa A (Case No. 4), a child aged 3 years, who died on her fourteenth day of illness.

Sections of bone marrow, spleen, and lymphatic gland were examined. The marrow was of a dark pink colour, and of soft consistence.

Microscopic examination of film preparations and of sections gave practically the same results. In the latter the capillary spaces were regular, and well formed. There was very marked cellular hyperplasia, and fat cells were very scarce. Polymorpho-nuclear cells were rarely noticed, but many transitional forms in various stages were seen. A few nucleated red blood corpuscles, and an occasional eosinophilic myelocyte were observed. Giant cells were present in relatively small numbers, but they were of such a striking character that they could not be overlooked. These cells were very large, with hyaline protoplasm and irregular convoluted nuclei, which stained very deeply, and were sometimes broken up or degenerated. Mitotic figures were only very occasionally observed. Phagocytosis within the myelocytes was not infrequent, the included cells being mainly red blood corpuscles.

Lastly, special attention must be drawn to the presence in the marrow of this case of a large number of diplococci. They were mainly extracellular, but occasionally they were observed in the interior of the phagocytes. These organisms probably gained access to the marrow immediately before or just after death. This was the only case of those observed in which organisms were detected in the bone marrow.

The spleen was enlarged and hyperemic, but of fairly firm consistence. The malpighian bodies were not markedly prominent. The sections showed an abnormally large number of cellular elements, but the most striking feature was the extent of the phagocytosis taking place. All through the section phagocytes were seen full of red blood corpuscles, and, in some instances, fragmented white cells also were included. Nucleated red corpuscles were rare, and poly-

morpho-nuclear cells were few in number, although many of the sinuses and spaces in the pulp were full of blood. An occasional eosinophile corpuscle was seen. Myelocytes were absent. Giant cells were observed full of red blood corpuscles, but their occurrence was very rare. A careful search failed to discover any evidence of mitosis in any of the cells throughout the sections. Scattered throughout the sections there were many groups of large diplococci, but nowhere were these observed within the cells.

The lymphatic glands throughout the body were not enlarged. Microscopic examination showed a certain amount of cellular hyperplasia, the predominating cells being lymphocytes. There were also present many larger cells, oval or elliptical in shape, and probably endothelial in character, as they were present in larger numbers around the sinuses and at the margins of the sections. These cells evidently perform the function of phagocytes, for, in the section, a few were observed with two or three small lymphocytes included in their protoplasm. Each of these ingested cells had a clear digestive zone surrounding them. No polymorpho-nuclear leucocytes, nucleated red cells, eosinophiles, nor micro-organisms were observed.

CASE III. The third case is that of Mrs. S. (Case No. 6) who died on her fifteenth day of illness.

The bone marrow and spleen from this case were examined. The marrow was reddish pink in colour, and of soft consistence. The films made from this marrow were unsatisfactory. Examination of sections showed that the capillary spaces were well formed and regular, that fat cells were scarce, whilst there was much cellular hyper-

plasia. Polymorpho-nuclear cells were scarce, but many transitional forms were observed. Careful search discovered mitosis going on here and there in some of the cells, but it did not occur very frequently.

An occasional eosinophilic myelocyte, and small numbers of phagocytes containing red blood corpuscles were observed. The number of giant cells was the most striking feature; they were present in relatively large numbers, and all possessed a large and highly convoluted nucleus which stained very deeply. The nucleus in some cases was broken up, probably undergoing degenerative or disintegrative changes, and apparently none of these cells were acting as phagocytes. No micro-organisms were observed.

The spleen was much enlarged, and of a dark purple colour. It was of very soft consistence and easily torn, and there was no marked prominence of the malpighian bodies. Microscopic examination showed a very marked cellular hyperplasia.

The most striking feature, however, and one which attracted immediate attention was the extent of the phagocytic action observed. The phagocytes were very numerous, and contained chiefly red blood corpuscles, though other cells, apparently lymphocytes, were included. Polymorpho-nuclear cells were few in number, and nucleated red blood corpuscles only occasionally observed, whilst eosinophiles and giant cells were not noted at all. The sinuses and vessels were filled with blood to a greater extent than in the previous cases. None of the cells were observed to be undergoing division, although careful search was instituted for mitotic figures. There were no micro-organisms.

CASE IV. The fourth case is that of Nellie S. (Case No. 9), who died on her twenty-first day of illness. It is of importance to note that this is the patient who had gangrene of the lung as a complication of her fever.

The bone marrow and spleen from this case were examined. The marrow was of a darkish red colour, and of fairly firm consistence. Examination of film preparations and of sections showed that a certain amount of cellular hyperplasia was present, but it was not so marked as in the specimens of marrow taken from other cases. Polymorpho-nuclear corpuscles were rare, but many transitional cells were present. Eosinophilic myelocytes were relatively common, and more frequent than in any of the other cases noted. Nucleated red corpuscles were also more frequent, and giant cells were relatively common, whilst the number of fat cells present showed that these were much less reduced in number than in the former cases. In striking contrast to some of the cases already detailed, no phagocytosis whatever was observed, and blood was more plentiful in the vessels and sinuses. Few examples of mitotic figures were observed, and no micro-organisms were noted.

The spleen was enlarged and hyperemic, but of firm consistence. The malpighian bodies were somewhat prominent. The section showed much cellular hyperplasia of the usual type. Phagocytosis was actively going on, both leucocytes and red blood corpuscles being ingested. Polymorpho-nuclear cells were frequently observed, a contrast being thus drawn between this spleen and those already described, in all of which polymorpho-nuclear corpuscles were scarce.

Another feature of this section was the number of giant cells:

these were present in relatively larger numbers than in any of the other spleens examined, and in some instances they were acting as phagocytes. Nucleated red cells were comparatively rare, and careful search had to be made before any eosinophile corpuscles were discovered. Blood was plentiful in the vessels and pulp spaces. As in the other cases, mitosis was looked for, but in none of the cells was there any evidence of this phenomenon. No micro-organisms were observed.

CASE V. Mrs. E. (Case No. 11), died on her twelfth day of illness. This was one of the most malignant cases of the series, and the post mortem appearances were very striking.

The spleen and bone marrow were examined. The latter when expressed from the rib was of a dark red colour, and of very soft consistence, so that it broke up into small pieces when dropped into the fixing solution. Sufficiently large pieces, however, were obtained for section cutting.

Microscopic examination showed great cellular hyperplasia, and a scarcity of fat cells. Polymorpho-nuclear corpuscles were also scarce, but there were many transitional forms in various stages. Giant cells were present, and at once attracted attention, not so much by their numbers, as by their great size and highly convoluted nuclei. The nuclei stained very deeply, and, in some instances, were broken up and evidently undergoing disintegrative changes. A few eosinophilic myelocytes were observed. These occurred with about the same frequency as the giant cells.

A certain amount of phagocytosis was taking place, the ingested

cells being principally red blood corpuscles. Blood was plentiful, but nucleated red corpuscles were very scarce. Mitotic figures were not abundant, and there were no micro-organisms.

The spleen was much enlarged, of a dark red, almost purplish colour, and exceedingly soft; indeed it was so diffluent that the pulp oozed out in a semi-fluid condition when the capsule was divided.

Examination of the sections showed an abnormally large number of small mono-nuclear cells. Blood was plentiful, but nucleated red corpuscles were not observed with any frequency. Polymorpho-nuclear corpuscles were scarce, whilst no giant cells and no eosinophile corpuscles were noted.

The most striking feature was the large number of phagocytes. These cells were more frequent around the sinuses, but they were active throughout the whole section, their contents being mainly red blood corpuscles. Occasionally mitotic figures were observed in cells which resembled phagocytes, but when division was thus taking place, the phagocytic function was apparently suspended. No micro-organisms were detected.

CASE VI. The sixth and last case is that of Thomas B. (Case No. 17), who died on his tenth day of illness. This was another very malignant case, and death occurred within 24 hours after admission to hospital. The spleen, bone marrow, and lymphatic gland were examined.

The bone marrow was of a dark pink colour, and of normal consistence. The appearances under the microscope were very striking.

The large number of giant cells at once attracted attention; these cells were in relatively greater numbers in this marrow than in any of the others previously examined. Besides this, many of them were acting as phagocytes, and contained red blood corpuscles. Others again had their deeply stained nuclear matter broken up as if undergoing degenerative changes.

Another striking character was the large number of phagocytes present. Phagocytosis had been observed in the marrow cells of the other cases examined, but, in this case, it was much more in evidence, the red cells mainly being taken up by the phagocytes. There were few fat cells, and polymorpho-nuclear corpuscles were scarce, but many transitional forms in various stages were present. Blood was plentiful, but few nucleated red corpuscles were noted. Occasionally an eosinophilic myelocyte was observed. Many of the ordinary marrow cells showed marked nuclear degeneration. Mitotic figures were not observed with any great frequency.

The spleen was much enlarged, and hyperemic. Its pulp was very diffluent, and the malpighian bodies were somewhat prominent. Examination of sections showed the presence of an abnormally large number of cells. There were a few polymorpho-nuclear corpuscles, and an occasional eosinophile, whilst at least one giant cell was observed containing many red blood cells.

The most striking feature, however, was the extent of phagocytic action. The inclusions consisted chiefly of red blood corpuscles, and in many instances of leucocytes and other degenerated cells. Blood was plentiful in the sinuses and spaces, but nucleated red corpuscles were very infrequent. Mitosis was not observed in

any of the cells of the spleen, and no micro-organisms were detected.

None of the lymphatic glands throughout the body were enlarged. Microscopic examination of sections showed that there was a certain amount of cellular hyperplasia especially as regards the lymphocytes. There were, however, many larger non-granular cells of a rounded, oval, or elliptical shape, with large nuclei and abundant protoplasm. These are the cells mentioned in the other cases as being most probably of endothelial origin, as they were in greater numbers at the margins of the sections and around the lymph spaces and sinuses. In one or two instances these endothelial cells were acting as phagocytes, but none contained red blood corpuscles. Polymorpho-nuclear cells were observed, but they were in relatively small numbers. No eosinophile corpuscles were noted, and although careful search was made for mitotic figures, none of these were observed. The vessels throughout the section were full of blood. There were no micro-organisms observed.

The details of the examination of the principal blood-forming organs in the foregoing cases furnish some data from which the chief facts may be elicited and general conclusions drawn.

A study of the marrow in typhus fever is of great interest on account of the relatively rapid course of that disease, and because, in view of that fact, it may be assumed that the condition before the onset of the disease is a comparatively healthy one.

Six cases in all were examined; four of these died before or at the crisis, and two (Cases 1 and 4) after that phenomenon had occurred. The ages of the patients varied from 1½ to 56 years.

DESCRIPTION OF PLATE III

Section of Bone Marrow from Case No. VI showing Giant Cells with large, convoluted, and deeply stained nuclei.

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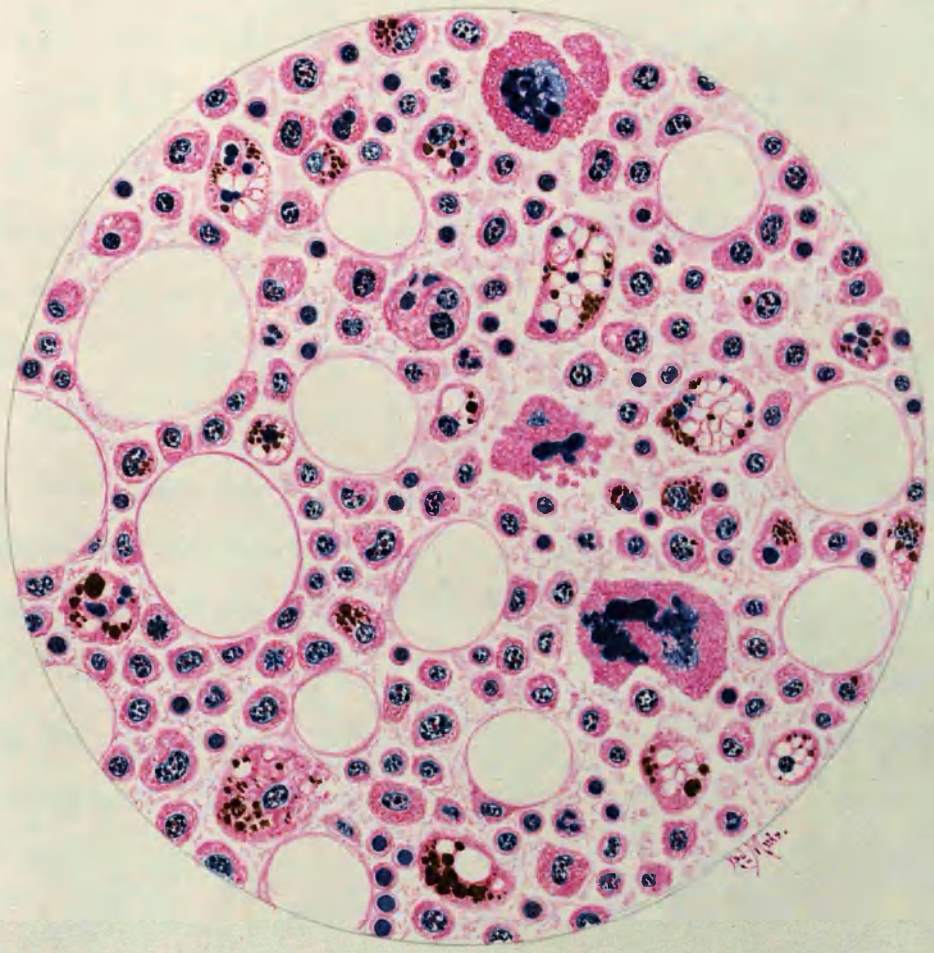

In all the cases examined there was a marked change. The ordinary marrow cells were very much increased in numbers, and there was a proportionately marked decrease in the number of fat cells. The diminution of fat indeed was so extreme that in some instances only a few solitary cells were observed throughout the section. Polymorpho-nuclear cells were present in every case, but they were usually very scarce. Eosinophile corpuscles do not disappear altogether from the bone marrow as they do from the blood of fatal cases. As a rule they are very scarce, only one or two it may be, occurring in a section. In one case, however (Case IV), these cells were relatively common; this was the patient who died a few days after her crisis from gangrene of the lung, so that it may be inferred that in this case the pulmonary complication, and not the typhus poison, was the factor mainly concerned in the presence of eosinophiles in the marrow. The eosinophile corpuscles are in all cases mononuclear, that is to say, they belong to the class of eosinophilic myelocytes. In no instance were these corpuscles observed to be undergoing division. Giant cells were present in all the marrows examined. They are of large size, and immediately attract attention. Their nuclei, as a rule, are convoluted and stain very deeply, thus indicating great condensation of the chromatin. The shape of the nucleus is very irregular, and in some instances it is broken up into separate pieces, or there may be several large fragments joined together by a thin filamentous strand. These cells are very much commoner in the more malignant cases, and in one case notably (Case VI) they were acting the part of phagocytes, and apparently digesting red blood corpuscles. Whether the fragmentation of the nucleus mentioned

above is an indication of division, or merely the result of degeneration of the cell is not very clear, but the latter is the more probable.

There was a fairly large amount of blood present in some cases, but it was mostly confined to the vascular channels. Nucleated red corpuscles were usually observed, but were never more numerous than normal; indeed they were apparently diminished. This diminution may be merely relative, however, and is accounted for by the great increase in the other cellular elements of the marrow. Phagocytosis was observed in two cases only (V and VI): these patients suffered from a malignant type of the disease, and although the phenomenon was present, it was not markedly active.

A great contrast may thus be drawn between the bone marrow and the spleen, where the phenomenon of phagocytosis is so marked and outstanding, that it immediately attracts attention. The cells occupied with this process in the marrow were large non-granular myelocytes, and in Case VI, some of the giant cells also were involved.

The occurrence of mitosis which is so characteristic of bone marrow in general, and which has been proved by Muir to be frequent in various infective conditions, was not observed with any great frequency in the typhus marrow. There were, however, many transitional cells in all stages of transformation from the mono-nuclear to the polymorpho-nuclear corpuscle.

The "neutrophile reaction" (this term is used by Muir to indicate an increase in the proportion of neutrophile myelocytes) in typhus is apparently not connected with the age of the patient, but has evidently some very definite relation to the severity of the toxemia. In the two most malignant cases (Cases V and VI), the neutrophile

reaction was much more marked than in the others, the cellular hyperplasia being very striking, and fat cells almost completely absent. On the other hand there was less cellular hyperplasia in the marrow of the younger patients, in whom the disease did not assume such a malignant character, although it proved equally fatal to all.

A parallel may now be drawn between the condition of the blood and that of the marrow. It is impossible, of course, to say what is the condition of the marrow during life in typhus fever, but the post mortem appearances give an indication as to what is taking place. It has been shown that there is a polymorpho-nuclear leucocytosis, and that these cells are relatively scarce in the marrow after death. The explanation given for this phenomenon, which has been observed in other diseases - pneumonia etc. - is that these cells apparently leave the marrow before death (Muir, Trans. Path. Soc. Lond., Vol. 53, part III, 1902). This explanation throws some light upon another phenomenon to which attention has been frequently directed in the section on leucocytosis, namely, the ante-mortem rise in the number of leucocytes. It would thus appear that the rise in the number of leucocytes in the peripheral circulation immediately before death, is principally due to the depletion of the bone marrow at that time of most of its polymorpho-nuclear cells. It follows naturally that the number of these cells thrown into the blood depends on the number stored up in the marrow, or on exceptional formative activity on the part of that tissue. It is probable, however, that these cells are not at any time stored up in the marrow, but are simply thrown into the circulation as they are produced, and that their production depends largely upon the severity

of the toxemia. The theory of chemiotaxis is naturally involved in this view, but it is now universally admitted that chemiotactic influence plays an important part in the migration and emigration of cells.

The condition of the marrow conforms to that of the blood in other important points, notably the presence of myelocytes and nucleated red corpuscles in the circulation.

Muir has shown that, in certain diseases, and more especially smallpox, where myelocytes and nucleated red corpuscles are comparatively numerous in the blood, their number is greatly diminished in the marrow; or, in other words, the neutrophile reaction is less marked. It will be remembered that myelocytes were very infrequent in the blood of the typhus patients, so much so that they were discounted altogether in the percentage calculation, and that nucleated red corpuscles were rare. The natural conclusion, therefore, is that the marrow in typhus fever ought to contain larger numbers of these cells. As regards myelocytes, this is exactly what obtains, for it has been shown that the neutrophile reaction of the marrow is very well marked in all the cases detailed. The nucleated red corpuscles, however, cannot be said to be increased in the bone marrow; this may be explained in the same way as the paucity of polymorphonuclear cells in the marrow was accounted for, that is by assuming that the red blood corpuscles are thrown into the circulation as soon as they are manufactured in the marrow. This assumption is supported by the presence of larger numbers of red corpuscles than normal in the peripheral circulation during life, a phenomenon which has been already remarked upon in the section upon leucocytosis.

DESCRIPTION OF PLATE V

Fig. 1. Section of Lymphatic Gland from Case No. II, showing normal condition of gland.

Fig. 2. Section of Spleen showing hyperplasia of cells, and absence of mitotic figures.

Does it show these?

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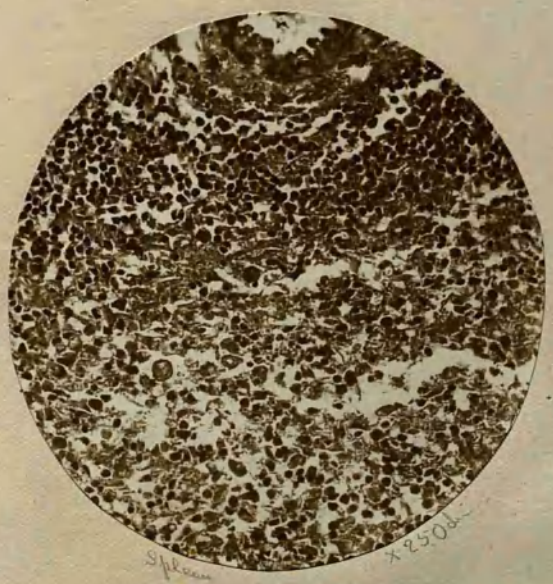

With regard to eosinophile corpuscles in the marrow and blood, the observations in typhus fever throw no light upon their origin, although Ehrlich states that these cells are formed in the bone marrow. He states also that substances which chemiotactically attract the polymorpho-nuclear cells are repellent to eosinophiles. This latter statement coincides with what is found in typhus fever, for it will be remembered that no eosinophiles were observed in the blood of the fatal cases of typhus, and that these corpuscles are present in very small numbers in the marrow. It may, therefore, be argued that the chemiotactic substance which attracts the polymorpho-nuclear cells from the marrow into the blood stream causes the eosinophiles to disappear from the circulation. As to the nature of the chemiotactic substance, it is probably the toxic substance produced by the specific cause of the disease, whatever that may be.

Another point to be noted is that there was no evidence of division of the eosinophiles in the marrow, or of their transition from the mono-nuclear to the polymorpho-nuclear form.

The changes in the spleen contrast markedly with those in the bone marrow. In all the cases examined the spleen was much enlarged, and usually deeply engorged and diffluent. The colour, of course, mainly depends upon the relative amount of red blood corpuscles present, but the swelling is chiefly due to cellular hyperplasia and to the accumulation of debris in the shape of degenerated blood corpuscles, as there is evidence of the destruction of both neutrophile leucocytes and red blood corpuscles in this situation.

In every case there was a marked cellular hyperplasia, the cells contributing to this being mainly of the small mono-nuclear

class. Polymorpho-nuclear corpuscles were scarce in most of the cases examined, but in one case (Case IV) they were observed with relative frequency; this was the patient in whom gangrene of the lung developed as a complication.

Eosinophiles were also very scarce, and in the majority of the cases were not observed at all; they were not present in greater numbers in the spleen of Case IV than in the others.

Giant cells were observed in all the cases examined, with one exception (Case III). These cells were readily seen on account of their size and their deeply stained convoluted nucleus. As a rule, they were present in very small numbers, but in Case IV they were observed in greater numbers and were acting the part of phagocytes, as many as half a dozen red blood corpuscles being included in one cell.

No myelocytes were observed.

Blood was present in large amount, especially in the sinuses and spaces, but nucleated red corpuscles were not observed with any frequency.

Phagocytosis was the most striking characteristic of the splenic cells, and was observed going on throughout the whole spleen. The red cells principally are taken up in the immediate neighbourhood of the sinuses, whilst the leucocytes are mostly absorbed in the pulp proper. The phenomenon of mitosis was not frequently observed in the spleen: indeed, it was noted in only two of the cases examined, and was confined to the hyaline leucocytes. Bacteria were present in the spleen of one case only, viz., Case II.

From a consideration of these facts it will be noted that the changes in the spleen fall naturally into two main groups, viz.,

1. destructive processes, and 2. proliferative changes. With regard to the former the characteristic feature of the splenic cells is their phagocytic activity. The cells concerned in this process are non-granular, and as stated before, composed partly of mono-nuclear leucocytes and partly of endothelial cells. Many degenerated cells are observed scattered throughout the pulp without any relation to the phagocytes, but it may be that these undergo extra-cellular digestion, a phenomenon which has been observed in all its stages by Muir, who states that not only leucocytes but also red blood corpuscles undergo extra-cellular disintegration in the spleen.

The removal of bacteria from the blood and their destruction by the cells of the spleen is another evidence of the phagocytic function of that organ, but its principal action appears to be corpuscular destruction. The spleen is thus shown to play an important part as a scavenger, by means of its phagocytic elements which remove the damaged and useless blood cells from the circulation.

Proliferative changes in the spleen are very rare, and only on one or two occasions were mitotic figures observed. These were confined to the hyaline leucocytes, and were never seen in any of the endothelial phagocytes. Another proliferative change, however, has been described, and importance attached to it by various observers. This is the formation of a distinct zone of cells around the malpighian bodies so that these become apparently enlarged. The cells forming this zone are of larger size than those forming the malpighian body proper and undergo active multiplication, as evidenced by the occurrence of mitotic figures. According to various French observers these cells multiply and acquire neutrophile granules

under the influence of stimuli from toxines, thus forming myelocytes which pass into the pulp and become polymorpho-nuclear leucocytes. Muir, however, disputes this statement, and, whilst agreeing with the French observers that there is a special proliferative layer of larger cells around the malpighian body, advances the suggestion that these cells pass into the pulp and there act as phagocytes, the process corresponding with what is seen in the lymph sinuses of lymphatic glands.

Careful search was made at the periphery of the malpighian bodies in the typhus spleens, but satisfactory evidence of the special zone alluded to was not found. There were certainly a few cells which were a little larger than the more central ones, but they did not form a distinctive zone, and there was no evidence of mitosis occurring in them. It is stated that the condition indicated is purely a pathological one, there being only very slight evidence of such a zone in the normal spleen. The spleen in typhus fever may, therefore, be one of the exceptions, as it may be presumed that the special proliferative zone around the malpighian bodies is not present in all infective conditions. In this connection it may be mentioned that no myelocytes which could be recognised as such were observed in the typhus spleens.

The presence of myelocytes in the spleen in infective conditions is considered of some importance, and evidently bears some relation to their presence in the peripheral circulation. Muir states that "in experimental infections, whenever they are present in the blood, they occur in proportionately greater numbers in the spleen, the appearance being as if this organ endeavoured to remove them from the blood." He also says that "observations on the human

spleen show that the occurrence of these cells in small numbers is comparatively common in infective conditions," and that "their presence, both in the blood and in the spleen, is usually associated with that of nucleated red corpuscles."

In view of the above statements, it would hardly be expected that myelocytes would be found even in small numbers in the spleen of typhus patients, for it has been already pointed out that these cells and also nucleated red corpuscles are very infrequently found in the peripheral circulation.

Nucleated red corpuscles too were not observed in the spleen in great numbers, so that the negative conditions of the typhus spleen, as regards myelocytes, correspond with the positive conditions of the spleen in other infections.

It is now generally admitted that the lymphatic glands of the body contribute certain elements to the blood which are known as lymphocytes, and that these corpuscles are thrown into the circulation in larger numbers than usual, under the influence of local stimulation. Apart from local stimulation, little is known except what has been gathered from clinical experience, as to the function of the lymphatic glands in the formation of the corpuscular elements of the blood. Ehrlich, however, considers the evidence thus obtained as sufficient to establish the theory that the lymphocytes of the blood are manufactured in the lymphatic glands and lymphatic tissue generally of the body. He holds also that lymphocytosis is produced by an increased flow of lymph through a more or less extended area of lymphatic tissue, so that, in consequence of the increased flow,

more elements are washed out of the lymph glands. The lymphatic glands are thus important factors in the production of leucocytes, and their examination along with the other blood-forming tissues is important.

In the present series only three cases were examined as to the glandular condition, but the results of these three examinations agree in all important particulars. The lymphatic glands of the groin were chosen as representative of the general lymphatic system.

There was no enlargement of any of the glands of the lymphatic system in the cases investigated; as there is no local infection, this might be expected except for a consideration of the fact that in infections due to other causes enlargement sometimes occurs. Although there was no evident enlargement, microscopic examination showed that, in all cases, there was a certain amount of cellular hyperplasia of the medulla, but that otherwise the tissue was apparently normal. The cells which were increased in numbers were mainly the ordinary lymph corpuscles. Other cells, oval or rounded, with large nuclei, and probably endothelial in origin were noted; these at times acted the part of phagocytes, ingesting both red corpuscles and lymphocytes. The process of phagocytosis, however, was uncommon.

Polymorpho-nuclear corpuscles which appear in large numbers in other infections (plague etc.) were observed only very occasionally in typhus, as if their presence were merely accidental. Eosinophile corpuscles are normally present in the lymphatic glands of some of the lower animals, and in certain abnormal conditions in the human subject, notably smallpox, they occur in comparatively large numbers. Some observers too are inclined to believe that the lymphatic gland,

and not the bone marrow, is the source of the eosinophile corpuscle, stating that they have observed them in the gland before their appearance in the marrow.

In the lymphatic glands of the typhus cases, no corpuscles of the eosinophile type were present, nor was there any evidence that might lend support to the theory of the lymphatic gland as the source of these cells.

It will thus be seen that the results of a study of the lymphatic glands in typhus fever are mostly negative, and throw but little light on the special leucocytosis of that disease.

The changes in the blood-forming organs in typhus fever may be now briefly summarised in the following statements:-

1. The bone marrow is the seat of a well-marked neutrophile reaction, and is
2. The chief manufactory of the polymorpho-nuclear neutrophile corpuscles
3. The spleen acts as a scavenger, its main function being that of phagocytosis
4. The lymphatic glands are practically normal.

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APPENDIX

APPENDIX

AGGLUTINATION REACTIONS

It is now well known that the agglutination reaction which results from the contact of serum from a person suffering from an attack of typhoid fever, with a young culture of the typhoid bacillus, may result from the contact of sera taken from persons suffering from diseases other than typhoid, and the question naturally presents itself whether a similar agglutinative power is possessed by the serum of a person suffering from typhus fever. The observations to be submitted were instituted with the object of throwing some light on this point.

The serum employed was obtained from blisters produced by the action of blistering tissue, and the epidermis previous to the removal of the serum by Pasteur pipettes was carefully sterilised. When not used immediately the pipettes were sealed at both ends, and preserved for future use. The observations on agglutination were carried out on the hanging drop, and in each experiment three degrees of dilution were employed, viz., 1 in 10, 1 in 20, and 1 in 60.

Experiments were carried out with serum taken from 55 cases of typhus. In fifteen the observations were taken immediately after the collection of the serum, but in the others the age of the serum varied considerably, being in some cases at least six months old, a

fact which may account for want of uniformity in result, as there seems little doubt that serum loses, to some extent at least, its agglutinative properties when kept for too long a time.

The appended table gives details of the observations made upon serum taken at different stages of the illness.

A complete reaction is indicated by the positive sign x , whilst the negative sign —— indicates that no reaction has taken place. Partial or incomplete reactions are indicated by the sign x p. (partial).

The cases examined were all undoubtedly typhus, and in six the disease ended fatally. We will first consider the reaction of serum taken from patients after the crisis.

In the fifteen cases where the serum was examined within a few hours after withdrawal from the blister, a positive reaction was obtained in eleven within a two hours' time limit, with a dilution of 1 in 10, and in eight of these the reaction was complete in forty minutes. With a 1 in 20 dilution complete agglutination was observed in two of these fifteen cases within two hours, whilst in the others a few clumps only - partial agglutination - were observed. In no case was there a complete positive reaction with a 1 in 60 dilution in the space of 24 hours.

In the remaining 39 cases, the serum from which was used after a period varying mostly up to six months, and in a few instances up to eighteen months, no agglutination was observed with a 1 in 60 dilution in twelve hours, whilst in twenty-four hours there was no appearance of clumping whatever with higher dilutions.

Serum taken during the acute phase of the disease was not found

so active as that taken after the crisis: in no case was a complete positive reaction obtained even after twelve hours' contact with the strongest dilution (1 in 10).

From the point of view of a differential diagnosis between typhus and enteric fever, the agglutination test appears to be of some value, inasmuch as in typhus fever it is only with very low dilutions (1 in 10) that any striking positive result is obtained within a reasonable time.

Bearing in mind that serum may manifest agglutinating properties when taken from a patient many years after he has passed through an attack of typhoid fever, it might be objected that the patients above referred to, whose serum gave a positive reaction, might have passed through an attack of this disease within a comparatively recent date, but careful enquiry made it possible to completely exclude this source of error, and the reactions, so far as they go, may be regarded as entirely dependent upon the action of the uncontaminated typhus serum.

In about a dozen cases the bacillus coli communis was substituted for that of typhoid fever. The results were very similar, that is to say, with a 1 in 10 dilution complete agglutination occurred within two hours, whilst with higher dilutions - 1 in 20, and 1 in 60 - a very much longer time was necessary for even a partial agglutination to occur.

TABLE OF AGGLUTINATIONS

No.	Day of Illness	Dilution 1 in 10	Time Mins.	Dilution 1 in 20	Time Hrs.	Dilution 1 in 60	Time Hrs.
1	19	x	40	x	2	—	24
2	21	x	40	x	2	—	
3	16	x	½ Hrs.	x p.	3½	—	
4	21	x	½	x p.	24	—	
5	17	x	½	x p.	24	—	
6	24	x	½	—	24	—	
7	38	x	2	x p.	12	—	
8	26	x	2	—	24	—	
9	16	x	2	x p.	2	—	
10	15	x	24	—		—	
11	35	x p.	12	—		—	
12	12	x p.	24	—		—	
13	55	x p.	9	—		—	
14	4	x p.	2	—		—	
15	14	x	8	—		—	
16	9	x p.	9	—		—	
17	10	x p.	9	—		—	
18	16	x p.	12	—		—	
19	15	x p.	12	—		—	
20	16	x p.	12	—		—	
21	15	x p.	12	—		—	
22	15	x	4	—		—	

TABLE OF AGGLUTINATIONS Contd.

No.	Day of Illness	Dilution 1 in 10	Time Hrs.	Dilution 1 in 20	Time Hrs.	Dilution 1 in 60	Time Hrs.
23	28	x p.	24	—	24	—	24
24	29	x p.	24	—		—	
25	37	x p.	24	—		—	
26	31	x	24	—		—	
27	19	x p.	24	—		—	
28	35	x p.	12	—		—	
29	15	—		—		—	
30	3	—		—		—	
31	6	—		—		—	
32	30	—		—		—	
33	14	—		—		—	
34	25	—		—		—	
35	48	—		—		—	
36	29	—		—		—	
37	36	—		—		—	
38	12	—		—		—	
39	43	—		—		—	
40	16	—		—		—	
41	35	—	24	—		—	
42	13	—		—		—	
43	18	—		—		—	
44	22	—		—		—	

TABLE OF AGGLUTINATIONS Contd.

No.	Day of Illness	Dilution 1 in 10	Time Hrs.	Dilution 1 in 20	Time Hrs.	Dilution 1 in 60	Time Hrs.
45	13	—	24	—	24	—	24
46	16	—		—		—	
47	14	—		—		—	
48	9	—		—		—	
49	10	x p.		—		—	
50	8	x p.		—		—	
51	9	x p.		—		—	
52	9	x p.		—		—	
53	13	x	½ Mins.	x	2	—	
54	6	x	40 Hrs.	x		—	
55	8	x	½	x		—	

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